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THE COURSE OF SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD*

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IN 1936 observations were reported[1] on the effects of liver therapy in 172 pernicious anæmia patients, in 74 of whom subacute combined degeneration of the spinal cord had developed. These patients had been admitted to the Toronto General Hospital between June, 1926, and December, 1933. On review in 1935, it was found that 57 of the 74 patients with subacute combined degeneration had shown marked or moderate improvement in their neurological symptoms and signs under adequate liver therapy. The most striking recoveries were observed when the interval between the onset of neurological disease and the institution of therapy was relatively short, *i.e.*, less than six months. Signs of long duration (two years or more) showed less striking change. The initial improvement had been maintained in every instance when the prescribed treatment was taken, and it was our opinion that it was due in large part to recovery in the function of damaged but not destroyed fibres in the tracts of the spinal cord and, to a lesser extent, to recovery from peripheral nerve involvement, which was usually a minor feature of the syndrome.

In the early years of liver therapy there was much difference of opinion about its effect on the neurological manifestations of the disease. Certain authors[2, 3, 4] doubted that improvement in the neurological symptoms and signs could be expected from liver therapy, and considered that it might not even prevent progression of the disease. Others[5 to 8] found that adequate liver therapy prevented progression and produced varying degrees of subjective and objective improvement in most patients. Gradually this latter opinion has become more generally accepted,[9 to 15, 20, 22] but some[16 to 19] attribute the improvement solely to recovery from peripheral nerve involvement and to training and re-education, doubting that any recovery of function in the affected fibre tracts of the spinal cord is possible.

We have not encountered any follow-up study based on observations over many years, and it was felt that a further survey of our original group of patients, who have been followed over periods of from 17 to 24 years, might disclose useful information about prognosis, including the effect of advancing age upon the disease, and also help to determine the long-term requirements of liver in treatment.

Scope

The present study consists chiefly of a survey of the survivors of the original group of 172 patients (see Table I). Most of these were followed continuously at the pernicious anæmia clinic of the Toronto General Hospital. Some have been under the care of outside physicians who co-operated by allowing periodic examination at varying intervals. In a number of instances the fate of patients that could not be located was determined by consulting the vital statistics of the Province of Ontario. It is interesting to note the causes and age of death in deceased patients.

For comparison with the original group, the patients with pernicious anæmia admitted between 1933 and 1946 have been surveyed and the surviving patients re-examined when possible.

Treatment of Patients Studied

In 1933, when potent crude liver extracts became available for intramuscular use, the treatment of pernicious anæmia underwent a

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TABLE I.

GENERAL SUMMARY OF FOLLOW-UP OF 172 PERNICIOUS ANÆMIA PATIENTS ADMITTED TO THE TORONTO GENERAL HOSPITAL BETWEEN JUNE, 1926, AND DECEMBER, 1933

A. *Original group*—172 patients:
- 74 had subacute combined degeneration when first seen or suffered development of subacute combined degeneration prior to December, 1933.
- 98 had pernicious anæmia without gross neurological disease.

B. *Status at general follow-up in 1947:*
- 10 patients—whereabouts unknown.
- 162 patients traced:—
  - (1) 69 patients or original groups with subacute combined degeneration:
    - 16 died of subacute combined degeneration, 1926-1933.
    - 2 died of other causes, 1926-1933.
    - 51 alive in 1934:
      - 7 died of subacute combined degeneration after 1934 (see Table III).
      - 16 have died of other causes.
      - 28 alive in 1947.
  - (2) 93 patients of original group with pernicious anæmia without gross neurological disease:
    - 23 died of pernicious anæmia, 1926-1933.
    - 11 died of other causes, 1926-1933.
    - 59 alive and free from subacute combined degeneration in 1934.
      - 1 died of pernicious anæmia and subacute combined degeneration after four years without liver. (See J.G., p. 298)
      - 4 died of pernicious anæmia. (See Table III.)
      - 22 died of other causes; in one subacute combined degeneration developed. (See B.N., p. 298)
      - 32 alive in 1947; in four of these subacute combined degeneration developed. (See pp. 297 and 298).

great change. Prior to this time our patients had depended upon the daily ingestion of one-third to one-half pound of whole liver, or liver broth or extract from 1,000 grams of liver. From 1933 to 1937 a relatively crude extract was used intramuscularly, 10 c.c. of which was derived from 200 gm. of liver. Patients with uncomplicated pernicious anæmia were given 10 c.c. per week intramuscularly, an early and excellent response being obtained; patients with subacute combined degeneration of the cord received double this dosage. In 1937, more concentrated and less irritating preparations became available, and since that time the extract has been increasingly purified.* On intramuscular administration of 0.5 to 1.0 c.c. per week, patients have shown maximal hæmatological responses; the usual dose for patients with subacute combined degeneration has been 2.0 c.c. per week; 4.0 c.c. has been used in some severe cases or in patients with symptoms of long duration. At first this dosage was continued indefinitely but for ten years, or more, it has been customary to lengthen the interval between injections to two weeks after one or two years' therapy if the patient appears to have reached maximal improvement, and in a number of cases longer intervals have been tried.

* Connaught Laboratories liver extract has been used throughout. This extract is claimed officially to have 15 units per c.c.; in our hands it was assayed at 20 to 25 units per c.c..

RESULTS

The present status of 162 of the original 172 patients is known, including 69 of the patients who had spinal cord degeneration at the time of the former report[1] (see Table I). Many are now dead, and it is interesting to note that as many of this original group died between 1926 and 1933 as between 1933 and 1947. Moreover, during the former period most of the patients died of pernicious anæmia and its complications, whereas, after the introduction of intramuscular liver therapy, most of the deaths were due to other causes. The high mortality prior to the introduction of intramuscular therapy was due, of course, to the inability or unwillingness of patients to take an adequate amount of liver by mouth. Many of these patients died shortly after coming under observation. As the group aged, the mortality from other causes naturally increased, but deaths from pernicious anæmia fell off because of the more satisfactory treatment.

Twelve patients, including eight with subacute combined degeneration, died from pernicious anæmia or subacute combined degeneration in the past thirteen and a half years (see Table II). Data regarding the regularity of treatment in these cases is presented in Table III. It will be noted that in all cases, often because of a psychosis or personality changes associated with age or serious organic disease, liver therapy was refused for long periods before the fatal termination.

Of the 51 patients listed in Table II as dying of causes other than pernicious anæmia and its complications, cardiovascular disease and carcinoma were the commonest causes of death. The sites of carcinoma varied, but seven patients died of carcinoma of the stomach, representing 14% of the deaths. This contrasts with a rate of 3% in a series of 4,000 consecutive autopsies

at the Toronto General Hospital. The incidence of carcinoma of the stomach in the patients with pernicious anæmia controlled by treatment is similar to that described by Kaplan and Rigler[21] in a recent statistical study. They record an incidence of 12.3 per cent in a large series of autopsies on patients with pernicious anæmia, which was three times as great as the incidence found at autopsy in people of the same age group.

Development of Subacute Combined Degeneration in Patients Formerly Free From Neurological Complications

Of the 59 patients of the original group who were alive and free from neurological complications in 1934, subacute combined degeneration developed in six between 1933 and 1947. In every instance the onset of neurological symptoms was preceded by a long period in which liver treatment was neglected or grossly in-

Table II.

Deaths Among 162 Patients with Pernicious Anæmia, Admitted to Hospital Between 1926 and 1933, During Periods on Oral and Intramuscular Liver Therapy.

	Died of pernicious anæmia and its complications		*Died of other causes*		
Period	*Pernicious anæmia with no neurological disease*	*Pernicious anæmia with subacute combined degeneration*	*Pernicious anæmia with no neurological disease*	*Pernicious anæmia with subacute combined degeneration*	*Total*
June, 1926, to December, 1933					
7½ year period of oral therapy	23	16	11	2	52
January, 1934, to June, 1947:					
13½ subsequent years of intramuscular therapy	4	8	22	16	50
Total	27	24	33	18	102

Table III.

Summary of Data, Age, Duration and Regularity of Treatment of the 12 Patients that Died of Pernicious Anæmia and its Complications after the Introduction of Intramuscular Liver Therapy in 1934

Patient	*Year of first admission*	*Diagnosis*	*Year of death*	*Age at death*	*Cause of death*	*Remarks*
I.L.	1926	Pernicious anæmia with subacute combined degeneration.	1946	77	Pernicious anæmia and subacute combined degeneration.	Refused all liver treatment in last seven years.
W.W.	1930	Pernicious anæmia with subacute combined degeneration.	1935	60	Subacute combined degeneration.	No liver therapy in last four years.
M.W.	1930	Pernicious anæmia with subacute combined degeneration.	1942	79	Subacute combined degeneration.	Became sensitive to liver several years ago and thereafter refused liver therapy.
W.G.	1930	Pernicious anæmia with subacute combined degeneration.	1940	85	subacute combined degeneration plus fractured femur and associated complications.	No liver therapy for several years.
L.M.	1931	Pernicious anæmia with subacute combined degeneration.	1945	74	Subacute combined degeneration plus fractured femur.	Refused liver therapy in last four years.
F.D.	1932	Pernicious anæmia with subacute combined degeneration.	1938	83	Subacute combined degeneration plus intestinal obstruction.	Refused liver therapy in last four years.
M.T.	1932	Pernicious anæmia with subacute combined degeneration.	1938	78	Subacute combined degeneration plus senile psychosis and fractured femur.	Refused liver therapy in last year.
J.E.	1933	Pernicious anæmia with subacute combined degeneration.	1934	61	Subacute combined degeneration plus psychosis.	Died in mental hospital; refused liver therapy in last year.
J.G.	1932	Pernicious anæmia with subacute combined degeneration.	1937	81	Pernicious anæmia plus senile psychosis.	Refused liver therapy last three years.
J.S.	1930	Pernicious anæmia.	1942	50	Pernicious anæmia plus paranoid psychosis.	Died in mental hospital; refused liver therapy in last four years.
E.H.	1932	Pernicious anæmia.	1942	64	Pernicious anæmia plus coronary thrombosis.	Refused liver therapy in last four years.
F.W.	1932	Pernicious anæmia.	1942	66	Pernicious anæmia plus chronic degenerative myocarditis.	Refused liver therapy in last five years.

adequate. Following are short case histories of these patients:

CASE 1

A.D., male. Pernicious anæmia was diagnosed in 1930 at the age of 42. He neglected liver therapy from 1930 to 1935, and symptoms recommenced in 1933. He was readmitted to hospital in 1935 with moderately severe subacute combined degeneration and showed remarkable improvement on massive liver therapy. Since discharge in 1935, he has been working as a labourer and has taken liver therapy regularly. He is subjectively free of symptoms although there is still (1950) objective evidence of posterior column involvement which has not changed since 1937.

CASE 2

L.P., female. Pernicious anæmia was diagnosed in 1931 when she was 47 years of age. She took liver by mouth irregularly until 1939 when moderately severe subacute combined degeneration developed. Since 1939, she has been under adequate treatment with improvement, and she is only mildly disabled at the present time.

CASE 3

M.G., female. Pernicious anæmia was diagnosed in 1932 when she was 61 years of age. She ceased to eat liver regularly in 1935 and, in 1936, subacute combined degeneration of the cord developed. With adequate intramuscular treatment there was both subjective and objective improvement which has been maintained, in spite of advancing years, on 2 c.c. of liver extract every two weeks.

CASE 4

B.L., female. Pernicious anæmia was diagnosed in 1932 when she was 39 years of age. Liver was taken by mouth, irregularly, from 1932 to 1946, but intramuscular therapy was refused. During this time she was hospitalized several times for recurrent depressive psychosis. In 1946, she began to have an unsteady gait and was found to have absent knee and ankle jerks, although vibration was well appreciated everywhere in the lower limbs. She still refused to take liver by injection but claimed to eat one-eighth pound of liver daily, and when last examined in 1947 her condition was essentially the same. The diagnosis of subacute combined degeneration was made, with some misgivings in this case because of the good appreciation of vibration in the lower limbs.

CASE 5

B.N., female. Pernicious anæmia was diagnosed in 1931 when she was 46 years of age. She took liver irregularly during 1932 and 1933; symptoms of subacute combined degeneration developed in 1933. When examined in 1934, the findings indicated moderately severe involvement of the posterior columns and pyramidal tracts. The patient attended the clinic regularly during the next three years, receiving the extract from 100 grams of liver every two weeks. This amount may have been inadequate for her, since examination in May, 1937, revealed no improvement and possibly slight progression of the neurological symptoms and signs, although repeated blood examinations had shown no abnormality. Thereafter, she received the extract from 200 grams of liver each week with gradual but progressive improvement, both subjectively and objectively, so that in 1942 the only persisting signs were absence of vibration sense in the lower limbs and of the right ankle jerk. She continued to take liver regularly and the improvement was sustained until she died suddenly of coronary thrombosis in 1944.

CASE 6

J.G., male. Pernicious anæmia was diagnosed in 1932 when he was 76 years of age. A senile psychosis developed and he took no liver from 1934 to 1937. He died in 1937 with advanced subacute combined degeneration which had become evident about one year previously.

There were eight others in the same group of 59 patients who received little liver therapy, in some instances for years, without the development of neurological manifestations. The explanation of this is obscure. At the present time all eight are taking what is considered to be adequate liver therapy and are well.

Of this group of 59 patients free from neurological disease in 1934, 32 were still living in 1947; in four (Cases 1, 2, 3 and 4 mentioned above), subacute combined degeneration had developed; the 28 others showed no manifestations of pernicious anæmia and were reasonably well in 1947. In May, 1950, one died at 83 years of age, and in June another died at 103 years of age.

PROGRESS OF PATIENTS WHO HAD SUBACUTE COMBINED DEGENERATION IN 1934

There are at present 32 living patients of the original group who have varying degrees of subacute combined degeneration. These include Cases 1, 2, 3 and 4 described above, in whom subacute combined degeneration developed after 1934, and the 28 survivors of the group who had subacute combined degeneration prior to 1934. The type of progress of the latter group is described in Table IV.

TABLE IV.

CHANGE IN SEVERITY OF THE CORD LESION IN TWENTY-EIGHT SURVIVING PATIENTS WHO HAD SUBACUTE COMBINED DEGENERATION IN 1934

Unchanged	*Worse*	*Improved*
15	5	8

Of the 15 patients whose neurological lesion was unchanged, three had experienced a short period of relapse following neglect of liver therapy; when therapy was reinstituted promptly there was a return to the original state. All five patients whose neurological state became worse neglected liver therapy for long periods.

An analysis of the *eight cases of subacute combined degeneration* showing improvement since 1934 indicates that improvement was both subjective and objective in every instance. The subjective improvement included decrease or disappearance of paræsthesiæ, recovery in strength and improved gait, and improvement of sphincter control. Objective improvement included improved power in the affected limbs, return of absent or sluggish tendon jerks, modification of abnormal plantar reflexes, lessening

of clonus and spasticity, recovery of impaired superficial sensation and postural sense, partial return of vibration sense, and improved gait.

In general, improvement in the signs and symptoms had occurred most strikingly in the first months or year after adequate treatment was commenced. Subjective improvement often continued over many years, although the neurological signs usually tended to remain stationary after the first couple of years. There were instances, however, when sensory and reflex abnormalities continued to show changes towards normal up to five years after the institution of adequate therapy.

In many of these patients other disorders unrelated to pernicious anæmia, frequently associated with advancing age, have developed. It was gratifying to find that, when these patients followed the prescribed treatment, they held their neurological gains.

As an illustration of the excellent response that may be made by a severe case of subacute combined degeneration and maintained up to an advanced age, the following case is described in some detail:

CASE 7

L.R., male, aged 54 years, first came under our observation in October, 1932, when he was admitted to the Toronto General Hospital. The history indicated that he had symptoms of pernicious anæmia seven years previously, but the diagnosis was not made until 1927. At this time, in addition to the symptoms of anæmia, he had severe paræsthesiæ in his limbs, weakness and difficulty in walking. Liver was taken by mouth, with some improvement in the symptoms referable to his upper limbs but weakness of the legs and unsteadiness in walking persisted. Six months before admission to hospital he began to have incontinence of bladder and bowel, and six days before admission he became unable to stand or walk.

On admission, the hæmoglobin was 71%, and the smear characteristic of pernicious anæmia. The patient looked older than his stated age of 54. His memory was poor for recent and remote events and his perception and attention were impaired. There was weakness of all four limbs, most severe in the legs which showed moderate spasticity; the ankle jerks were absent, and there were bilateral dorsiflexion responses on plantar stimulation. Sense of position and passive movement were grossly defective in the feet and toes. Vibration was not appreciated at or below the anterior superior spines. Superficial sensation was impaired up to the lower abdomen. The patient was completely incontinent of bladder and bowel.

He was given a fresh extract from 1,000 grams of liver daily but, for a time, his condition deteriorated. Bed-sores developed and he became very mentally confused. After a few weeks improvement became manifest and gradually continued. By February, 1933, he was mentally alert and emotionally stable. There was no abnormal finding in the upper limbs. The power and coordination of the legs were decidedly better than on admission, although weakness of the ankles was still sufficiently severe that he was unable to stand on his feet. The knee and ankle jerks could not be elicited. On plantar stimulation there was still bilateral dorsiflexion of the great toes. Postural sensation was improved in the right lower limb, but he was unable to appreciate the direction of gross movement of the left great toe. There was no return of vibration appreciation. The legs were still decidedly spastic and the patient was suffering from flexor spasms. Superficial sensation had returned partially over the sacral segments on the lower limbs. He had regained sphincter control but there was urgency and hesitancy on micturition and he was severely constipated.

In spite of the improvement in the neurological signs, flexion deformities of both legs began to develop at the knees and thighs. He received physiotherapy to counteract the contractures, and attempts were made to get him walking but without success. The increasing contractures led to the decision in April, 1933, to use orthopædic measures to control them. Under spinal anæsthesia, the legs were forcibly extended and plaster casts applied. By this means the angle at the knees was changed from 110 to 145 degrees. This procedure was repeated two weeks later, when it was possible to get the legs almost straight. Plaster casts extending up to the crotch were left *in situ* for several months, during which time the patient was encouraged to walk.

The casts were removed in September, 1933. There was still some flexion deformity of the thighs on the trunk, which caused him to walk with the trunk bent forward, and for a time flexor spasms would interfere with his sleep at night. However, his gait gradually improved so that he required progressively less support to walk or to stand. By August, 1934, he could walk well with one crutch. Power in the legs was greatly improved and the flexor spasms were very mild. Postural sense in the feet was much better and superficial sensation was almost normal.

The patient has continued under observation up to the present time and, with the exception of a period in the winter of 1936-37, he has attended the clinic regularly and received intramuscular liver extract as prescribed. Improvement continued gradually during the years of observation, being most apparent up to 1939. Subsequently the condition remained fairly stationary with no signs of any regression. In September, 1946, he was walking with a cane but could walk almost as well without it. The power was good in the lower limbs and the spasticity was not marked. The flexion deformity at the thighs was much less than in 1934; the knee jerks were present and active; ankle jerks were absent; plantar responses dorsiflexion. The gait showed a somewhat wide base, but the only defect in postural sense was a few mistakes on passive movement of the toes of very small range. Vibration was appreciated weakly at the ankles and toes. There was no impairment of superficial sensation. He had some occasional delay in initiating micturition and required to take laxatives for constipation, but otherwise there was no disturbance in the sphincter control. His condition was essentially unchanged in the fall of 1950.

This very severe case of subacute combined degeneration had a five-year history of the disease before receiving adequate treatment at the age of fifty-four. At 73 he is holding the improvement produced by liver therapy. Despite complications, such as moderately severe chronic multiple arthritis, essential hypertension, and symptoms of degenerative heart disease, the disability from the spinal cord disease after treatment became surprisingly small.

PROGRESS OF PATIENTS ADMITTED SINCE 1933

Between June, 1933, and December, 1947, there were 408 patients with pernicious anæmia admitted to the Toronto General Hospital. One hundred and seventy-seven of these patients had evidence of subacute combined degeneration of the spinal cord, a number of them having been admitted for treatment of the neurological lesion. Although the proportion of cases with

subacute combined degeneration is about the same as in the earlier group, the general tendency has been for uncomplicated patients to be treated at home; accordingly, those with spinal cord involvement may constitute a larger proportion than would otherwise be the case.

Of the 177 patients in whom subacute combined degeneration has been diagnosed since 1933, 144 were traced and the 88 survivors were examined. The findings in this group of cases substantiate what has been noted previously. The more acute cases showed the most rapid and complete recovery, whereas patients with long duration of symptoms before treatment was instituted showed less striking objective change although subjective improvement in paræsthesia, strength and ability to use the limbs was often marked.

In estimating improvement, the same criteria were used as formerly. Sixty-five of the 88 patients examined showed definite improvement as judged by changes such as increase in power, lessened spasticity, return of absent or diminished reflexes, better sphincter control and improvement in deep and superficial sensory disturbances. In eight of the cases, one or both plantar reflexes gradually changed from dorsiflexion to plantar flexion under observation. These results offer further strong evidence in support of the opinion, formerly expressed, that the improvement noted in such patients is largely a result of recovery of function of fibres in the involved tracts of the spinal cord which have escaped destruction and, to a lesser degree, of recovery from the peripheral nerve involvement.

A small proportion of patients who adhered to treatment showed little or no change in their neurological condition. These were cases of long standing before treatment was commenced. The patients who became worse were shown to have neglected treatment.

DISCUSSION

The above observations confirm the opinion previously expressed that, in patients with pernicious anæmia who receive adequate liver therapy, subacute combined degeneration of the cord does not develop; if subacute combined degeneration is already present before the institution of therapy, subjective and objective improvement will occur in the majority of cases. Advancing age in no way alters the prognosis, and the life expectancy of patients with pernicious anæmia and subacute combined degeneration is not diminished providing the prescribed treatment is maintained indefinitely. The average age, in 1947, of 60 survivors of the original group was 67 years.

It is interesting to consider the 21 deaths from subacute combined degeneration in the group admitted from 1926 to 1933 (see Tables I and III). Sixteen died prior to the introduction of intramusular liver therapy in 1934; 15 of these died either shortly after coming under observation or because of refusal to eat liver; one patient with very severe subacute combined degeneration took the liver therapy regularly but died of large infected bedsores and pyelonephritis which complicated the cord disease. The other eight patients (see Table III, patients 1 to 8) died since 1933, at an average age of 74; they all failed to take liver adequately for long periods.

Subacute combined degeneration is a characteristic syndrome of pernicious anæmia, and there is little difficulty in differentiating it from other neurological diseases. Our experience leads us to the opinion that peripheral nerve lesions are a minor feature of the disorder and that the major manifestations are due to degenerative lesions in the long fibre tracts of the spinal cord. The fact that great functional improvement, associated with disappearance of signs of the original disease, occurs as a rule in those cases of relatively short duration indicates that many of the fibres are capable of resuming active function when the lesion subsides under treatment. It is interesting also that in some cases moderately severe symptoms had persisted for several years, yet subsided gradually over a period of many months on well maintained therapy. It would appear that in such cases many fibres survived a long period when their function was grossly impaired by the active lesion and were able to regain normal function under liver therapy. That the improvement was not due simply to re-education and practice, important as they are, is indicated by the gradual change in the plantar responses and other organic signs to or towards normal.

One of the major difficulties in treatment of pernicious anæmia patients is to persuade them to adhere to treatment after the symptoms have subsided and they feel well. Occasionally patients may go for several years on inadequate

or even no liver therapy without development or relapse of neurological symptoms but in approximately half of such cases neurological symptoms will appear.

Patients in whom subacute combined degeneration fails to develop after long periods of inadequate treatment may have some mechanism which operates to protect the nervous system against the effects of the deficiency, whether or not there is early recurrence of the anæmia. The importance of maintaining adequate liver therapy in all patients cannot be over-emphasized however; six cases have been cited in which subacute combined degeneration developed as a result of neglect. One of these (Case 5, B.N.) is of considerable interest since, after development of subacute combined degeneration, she received a relatively small dosage of liver for three years, which proved to be inadequate for her as the neurological manifestations showed no improvement and perhaps slight progression. This suggests that the amount was almost sufficient to maintain the *status quo,* but not sufficient to effect improvement. Subsequently, when the dosage was greatly increased, there was remarkable and sustained improvement over a period of several years. Such observations indicate that a lesion of the fibre tracts, severe enough to give rise to disabling symptoms, may persist for a long time without actual destruction of fibres.

It was natural to wonder whether degenerative changes of age would so damage remaining intact fibres in the formerly diseased cords as to lead to a gradual deterioration of function. Fortunately this has not proved to be the case.

It has been clinical experience that infection may retard recovery from the anæmia of pernicious anæmia, and it seems to be true that under such circumstances larger dosage of the anti-anæmic principle may be required. It has been our experience that, in the recovery phase of subacute combined degeneration, overexercise to produce undue fatigue may lead to temporary aggravation of the symptoms, and sometimes infection seemed to have a similar effect.

During the long period of observation of our pernicious anæmia patients an attempt was made to find the lowest dosage of liver which would maintain the patient free of all symptoms and signs of the disease. With this purpose in view, a number of the patients who were attending the clinic regularly—most of them free from neurological disorders—had their doses reduced to one c.c. of concentrated liver extract (15 Units +) every four or even every six weeks. After a period of several years mild macrocytosis developed in a number of cases, but in no instance did cord disease appear of relapse. The occurrence of macrocytosis made us feel, however, that it was not safe to continue to treat patients with neurological involvement with injections at such long intervals. It was concluded that a safe maintenance dosage for patients with subacute combined degeneration was two c.c. (30 units) of liver extract every two weeks; patients free from any manifestations of subacute combined degeneration, under regular careful observation, may be treated with two cubic centimetres every four weeks, but one cubic centimetre at a fortnightly interval is regarded as preferable.

SUMMARY AND CONCLUSIONS

A follow-up study has been made of the 172 pernicious anæmia patients (74 with subacute combined degeneration of the spinal cord) that were admitted to the Toronto General Hospital between 1926 and 1933. A former report on this group was made in 1936.[1] The records of 408 pernicious anæmia patients (177 with subacute combined degeneration) admitted to the Toronto General Hospital since 1933 have also been analyzed. Most of the surviving patients of both groups have been under observation to the present time.

The findings in this study fully support the belief previously stated[1] that maintenance of adequate therapy will prevent the development of subacute combined degeneration in patients with pernicious anæmia and, if subacute combined degeneration is already present, its further progression will be prevented; in the majority of cases, marked subjective and objective improvement will occur. Failure to improve on adequate therapy was found only in patients with neurological symptoms of long duration.

The neurological improvement is due, in large part, to improved functioning of the reversibly affected fibres in the tracts of the spinal cord and, to a lesser extent, to recovery from peripheral nerve involvement. The improvement is most striking and complete when adequate liver therapy is instituted within several weeks or months of the onset of symptoms, but even after much longer intervals definite objective as well

as subjective improvement may take place, although it is likely then to be more gradual.

Attention is drawn to the variability shown in the susceptibility of the nervous systems of patients to inadequate liver therapy, and also to the possibility that treatment insufficient to cause improvement in function may protect involved fibres from destruction.

It is interesting that the neurological status of patients with subacute combined degeneration does not regress with advancing years provided that therapy is not neglected. It would appear, also, that treated pernicious anæmia patients, whether they have had subacute combined degeneration of the cord or not, have a normal life expectancy in spite of an increased incidence of cancer of the stomach.

It is difficult to know the optimal dosage of liver for patients with subacute combined degeneration. It is adequate, however, to give each week at least 30 units of liver extract (or, perhaps, the equivalent amount of vitamin B_{12}). This dosage should be maintained until further improvement in symptoms and signs has ceased and for at least one year. When the condition has been stationary for months the interval between injections may, with safety, be increased to two weeks. In the presence of severe prolonged infections, return to the weekly dosage may be desirable.

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REFERENCES

1. HYLAND, H. H. AND FARQUHARSON, R. F.: *Arch. Neurol. & Psychiat.*, **36**: 1166, 1936.
2. COHEN, A. E.: *J. A. M. A.*, **90**: 1787, 1928.
3. DAVISON, C.: *Arch. Neurol. & Psychiat.*, **26**: 1195, 1931.
4. GOLDHAMER, S. M., BETHEL, F. H., ISAACS, R. AND STURGIS, C. C.: *J. A. M. A.*, **103**: 1663, 1934.
5. DAVIDSON, S., MCCRIE, J. G. AND GULLAND, G. L.: *Lancet*, **1**: 847, 1928.
6. RICHARDSON, W.: *New England J. Med.*, **200**: 540, 1929.
7. STARR, P.: *J. A. M. A.*, **96**: 1219, 1931.
8. MEULENGRACHT, E.: *Ugesk. f. Laeger*, **95**: 819, 1933.
9. MILLS, E. S.: *Am. J. M. Sc.*, **191**: 72, 1936.
10. UNGLEY, C. C.: *Clin. J.*, **67**: 5, 1938.
11. DAVISON, C.: *Arch. Int. Med.*, **67**: 473, 1941.
12. HEILMEYER, L.: *Med. Klin.*, **38**: 169, 1942.
13. GOTTLIEB, R.: *Canad. M. A. J.*, **45**: 420, 1943.
14. RUNDLES, R. W.: *Blood*, **1**: 209, 1946.
15. HALL, B. E., KRUSEN, F. H. AND WALTMAN, H. W.: *J. A. M. A.*, **141**: 257, 1949.
16. CARMICHAEL, E. A.: *Proc. Roy. Soc. Med.*, **27**: 775, 1934.
17. GRINKER, R. R. AND KANDEL, E.: *Arch. Int. Med.*, **54**: 851, 1934.
18. WALSHE, F. M. R.: Diseases of the Nervous System, Livingstone, London, 1945.
19. COURVILLE, C. B.: Pathology of the Central Nervous System, Pacific Press, Los Angeles, 1945.
20. FOSTER, D. B.: *Arch. Neurol. & Psychiat.*, **54**: 102, 1945.
21. KAPLAN, H. G. AND RIGLER, L. G.: *Am. J. M. Sc.*, **209**: 339, 1945.
22. STURGIS, C. C.: Hæmatology, Charles C. Thomas, Springfield, 1948.

THE HEXAMETHONIUM COMPOUNDS IN THE TREATMENT OF HYPERTENSION

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IN 1948 two groups of British investigators[1, 1a] published a joint report of independent work on a new and interesting series of drugs, known as the polymethylene bistrimethyl ammonium (methonium) compounds. The generic formula of these compounds is represented in Fig. 1.

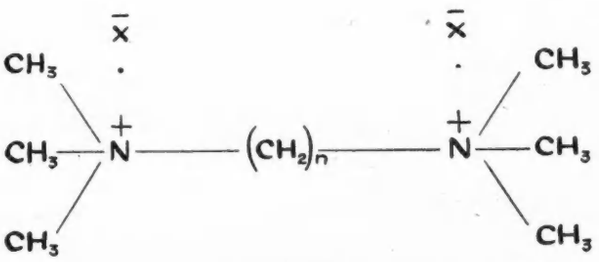

Fig. 1.—The generic formula of the methonium compounds.

The individual members of the methonium series are designated according to the number of carbon atoms in the polymethylene chain and are identified by the symbols C_n. The pharmacology of C_2 to C_{18} has been carefully studied by Paton and Zaimis,[2] and of these the most important members are C_{10} or decamethonium, which has a marked curare-like action in blocking neuromuscular transmission of nerve impulses, and C_5 and C_6, penta- and hexamethonium which have the ability to paralyze autonomic ganglia. This ganglionic blockade is much more effective than that produced by tetraethylammonium salts inasmuch as smaller doses of the methonium salts result in a paralysis lasting 3 to 4 times as long and the side effects are much reduced.

In animal and human investigation the biniodide and bibromide salts of penta- and hexamethonium have been principally used. Of these the bromide salts have been proved to be the more efficacious but recently because of reports of bromide intoxication bitartrate salts have been introduced.

Organe, Paton and Zaimis[3] were the first to show that in normal adults if 20 to 40 mgms. of C_5 were injected intravenously a fall in blood pressure occurred, especially if the subject was in the erect position. This was corroborated by Arnold and Rosenheim[4] who also noted changes in skin temperature following its use. These investigators then tried the effect of C_5 in 6 hypertensive patients and they noted a marked drop in blood pressure which would last for approximately one hour. Burt and Graham[5] carried out further investigations with penta- and hexamethonium injected intra-

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venously and they were impressed with the marked postural hypotension that could be induced in hypertensive patients. They also observed the peripheral vasodilatation but found that the rise in skin temperature readings was confined almost entirely to the legs where sweating was abolished.

The effects on gastric secretion of the methonium compounds were observed by Kay and Smith.[6] They found that after an intramuscular injection of C_5 to patients with active duodenal ulcers an achlorhydria could be produced which would last as long as 3 hours. They noted also a concomitant marked inhibition of gastric motility.

It was only logical that with the above findings the methonium compounds should be given a clinical trial in the treatment of patients with hypertension. Restall and Smirk[7] were the first to thus experiment and their results in 15 hypertensive patients receiving C_5 were encouraging and stimulating. In the past year a number of further studies have been reported on the use of these drugs in the treatment of hypertension. As is usual in the evaluation of any method of treating hypertension there has been considerable controversy in the reports, with some investigators being favourably impressed[8 to 12] while others[13, 14] appear doubtful of the methonium compounds. All observers are agreed that these compounds if given intramuscularly can cause a transient fall in blood pressure; however some doubt that this fall is beneficial to the hypertensive state. In view of the obvious importance of these drugs, if they are beneficial, we have attempted to give them a thorough clinical trial.

MATERIAL AND METHODS

This report is based on the use of hexamethonium compounds* in 31 patients suffering from hypertension.

All patients were admitted to hospital and blood pressure readings were taken every four hours for periods ranging from several days to several weeks prior to the administration of the drug. The patients, if able, were purposely not confined to bed but were allowed to be up and to do as much as they pleased. This was done in an attempt to avoid the fall in blood pressure which may accompany bed rest.

All patients were investigated as carefully as possible with electrocardiograms, chest x-rays, fundal examinations, blood and renal studies being done. The presence of pheochromocytoma was ruled out as necessary.

The vagaries of the hypertensive patient were kept in mind. Their tendency to show a marked drop in blood pressure with bed rest, an optimistic attitude of the physician and the reassurance and relief of tension afforded by hospital admission, are well known. To partially circumvent these factors our patients were arbitrarily divided into three groups. Firstly, those patients who showed no drop in blood pressure while under preliminary observation and who, in addition, revealed evidence of renal damage as indicated by abnormal urinary findings with fixation of urinary specific gravity, and most important of all, retention of nitrogenous end-products in the blood. Secondly, those patients whose blood pressure remained unchanged during the observation period but who revealed no signs of renal damage. Thirdly, a large group of patients who showed soon after admission marked fluctuations in blood pressure which in some individuals would on occasion fall to normal levels.

At first almost all patients were started on hexamethonium bromide by mouth, a 250 mgm. tablet being crushed and given before a meal as a test dose. The following day a 250 mgm. tablet was given 4 times and on subsequent days the dose was rapidly increased until 3 grams daily were being administered. During the first few days the patients were kept in a sitting position in bed so that if postural hypotension occurred it could be easily overcome by having the patient lie flat. Latterly 5 of our patients have been given hexamethonium bitartrate with a maximum daily dose of 4 grams. A few patients, as will be observed, have been given the bromide salt of C_6 by intramuscular injection.

After treatment was started blood pressure readings were taken from 4 to 12 times daily in the lying, sitting and where possible in the standing posture. Particular attention was paid to the occurrence of any toxic effects and after the first 3 or 4 patients bromide intoxication was carefully watched for and blood bromide determinations were made frequently.

RESULTS

Group 1.—This group comprised 6 patients. All had severe hypertension with marked impairment of renal function as manifest by albuminuria, fixation of urinary specific gravity and markedly elevated blood urea and creatinine levels. Four patients suffered from agonizing hypertensive encephalopathic attacks. Two

* The oral hexamethonium bromide and bitartrate preparations used in this study were generously supplied by Poulenc Limited, Montreal. Similarly the intramuscular hexamethonium bromide preparation used was generously supplied by E. R. Squibb & Sons, Trenton, N.J.

patients were considered moribund when treatment was instituted. They were extremely dyspnœic with evidence of myocardial failure which had failed to respond to the usual therapeutic measures.

Four patients in this group were given C_6 by mouth in small doses. All had a satisfactory drop in blood pressure without evidence of renal shutdown. All were relieved of their headaches and felt remarkably better. One patient who had had a previous sympathectomy for hypertension, without much benefit, stated that he obtained much more relief from the C_6.

The two patients who were so very ill were given small doses of C_6 by intramuscular injection, 15 mgm. being an average dose. The results in both patients were remarkable inasmuch as their blood pressure dropped to normal and within a few hours all their dyspnœa had disappeared. In this group there was no improvement noted in urea retention, one patient dying in uræmia after several months of treatment. The remainder are still doing remarkably well considering the seriousness of their original condition, with blood pressures remaining at low levels. All have now been followed for periods varying between two and eight months. In this group two patients developed hypotensive attacks while under therapy and one patient developed elevated blood bromide levels and was subsequently changed to the bitartrate preparation.

Comment.—In this group of patients there seems to be little doubt that the hexamethonium preparations are useful therapeutic aids. Their relief of symptoms was dramatic and there is no doubt in our minds that their life span has been prolonged.

It is interesting to note in other patients who had fixation of urine specific gravity with inversion of the day-night volume, but without retention of urea, no such dramatic fall of blood pressure occurred with C_6. This suggests that in patients with urea retention the hexamethonium compounds may be more slowly excreted and consequently a therapeutic effect is obtained with relatively small doses. In view of this possibility we would advise in this group that the dosage of hexamethonium bromide be limited to 1 gram daily, while parenterally not more than 50 mgm. daily should be given during the first week of therapy (Fig. 2).

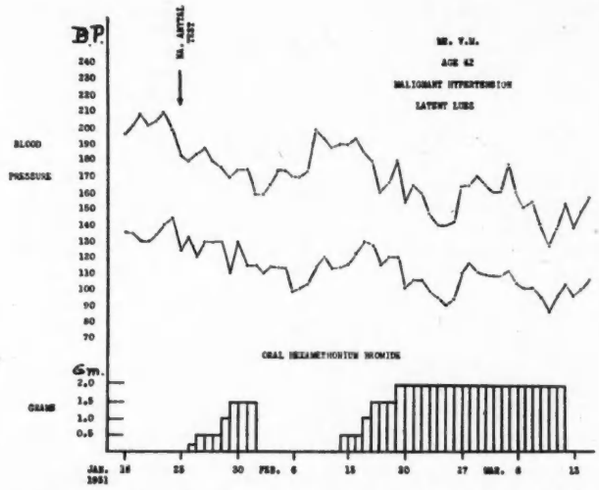

Fig. 2.—Blood pressure chart of a patient, male, age 42 years, suffering from "malignant hypertension". Note the initial fall in blood pressure when hexamethonium therapy was instituted with relatively small doses. When therapy was discontinued for a period of 10 days blood pressure returned to its original levels. When therapy was re-instituted for a prolonged period blood pressure was again lowered to normal levels.

Group 2.—This group contained 6 patients whose blood pressure readings remained constantly elevated despite hospitalization, bed rest and sedation. These patients were all severe hypertensives and all showed a similar psychological behaviour pattern in that they were extremely active, tense and hard-driving individuals. All were between the ages of 28 to 48 years. The only evidence of impairment of renal function in this group was a fixation of urinary specific gravity in 2 patients.

The patients in this group were all given hexamethonium bromide in maximum dosages of 3 grams daily and in none was any significant drop in blood pressure noted even on standing. Three patients were then given hexamethonium bromide intramuscularly in doses of 300 to 400 mgm. in 24 hours. With this dosage all had abrupt falls in blood pressure which never lasted more than one hour. Headaches could be alleviated in one patient by this transitory fall but he complained that the drug made him feel miserable. The 2 other patients of this group appeared to develop a tolerance to this medication in that continued administration produced a progressively diminishing lowering of blood pressure until they were considered unresponsive. One patient could not take more than 50 mgm. intramuscularly per dose because of resulting inability to void. It is interesting to note that none of these patients developed abnormal blood bromide levels and

none developed hypotensive syncopal attacks. A further feature of this group is that 3 of these patients left hospital against advice before parenteral therapy could be instituted.

Comment.—In this group of hypertensive patients who were all young, and in whom a psychogenic etiological factor seemed to predominate, the use of hexamethonium by mouth appeared to be of no value. Parenterally these compounds may be of limited value in affording temporary symptomatic relief but we do not believe that prolonged continuous administration of the drug is warranted. It is possible that intermittent therapy may be of value to overcome the rapid development of tolerance manifest by some patients of this group (Fig. 3).

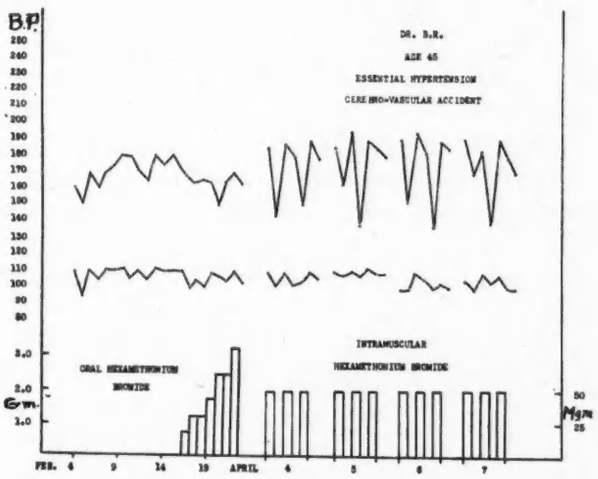

Fig. 3.—Blood pressure chart of a patient, male, age 45 years, suffering from "essential hypertension". Note the failure of blood pressure response to the oral administration of hexamethonium bromide. With intramuscular administration daily dips of blood pressure readings could be produced to nearly normal levels, but the effects were transitory.

Group 3.—This group of 19 patients presented several characteristics in common. They all showed a marked fall in blood pressure soon after hospital admission, even although they were not confined to bed. Their attitude was quite different from that of group two, as they were co-operative, relaxed and quite willing to stay in hospital. They still, however, showed the ravages of their hypertension, as 7 had had cerebral vascular accidents of various degrees, 4 had mild myocardial failure and one had severe angina pectoris. All showed varying degrees of hypertensive retinopathy and in all the electrocardiograms were abnormal.

These patients were given hexamethonium bromide or bitartrate by mouth for long periods ranging from 1 to 5 months. The immediate evaluation of the drug was difficult due to their fluctuating blood pressure, but the occurrence of hypostatic syncopal attacks in 5 patients was certainly a drug effect. We therefore relied on the presence or absence of a marked drop in blood pressure in the standing position, as compared with that noted on lying, as evidence of drug action, even though fainting did not occur. Levels as low as 90/65 were observed.

Fig. 4 exemplifies the extreme degree of blood pressure lability that may occur in this group.

We believe that in all these patients the hexamethonium resulted in the postural fall of blood pressure. We were impressed by the sense of well being experienced by the members of this group and we feel that their blood pressure readings after leaving the hospital have been on a lower level than those obtained prior to their admission.

In two patients interesting effects were noted on coincidental illnesses. In one of these the pain of a duodenal ulcer was relieved immediately after the drug was given, while in another intermittent claudication of a year's duration was improved greatly after a month's treatment of her hypertension.

Five patients who were taking hexamethonium bromide developed generalized malaise and in all an elevated blood bromide level was discovered. The highest blood bromide level noted was 80 mgm. %. These patients rapidly regained a sense of well being when they were changed to the bitartrate preparation.

Half of this group developed moderate constipation but this was easily overcome. Dryness of the mouth and visual defects did not occur.

In 2 patients serious vascular accidents occurred while under therapy. One developed a coronary artery thrombosis, while in the other a cerebral thrombosis occurred. Both of these patients had shown a dramatic postural hypotension some days after administration of the drug and had felt better, until the onset of the above episodes. Whether these accidents were accidental or whether they resulted from the blood pressure changes is difficult to state but their occurrence is warning that this group of drugs should only be used when the patient is under observation and preferably in hospital.

Comment.—It can be easily seen that the evaluation of any form of therapy in this group is bound to be open to criticism. It is probable that, in the past, the good results claimed for any treatment, whether medical or surgical, were obtained in a similar group.

Sixty-one per cent of our patients fell into this category. In such a small series this may not be of statistical significance but it is of interest that this figure closely approximates that of Bechgaard[15] who states that 60% of hypertensive patients improved temporarily on any form of therapy. Similarly as noted by Locket et al.,[14] Watkinson and Evans report a fall in blood pressure in 60% of their patients treated with thiocyanates while Kempner reports 70% of cases improved on the rice diet (although not all had a fall in blood pressure).

The long term observation of this group will be of great interest and may now be carried out with a greater margin of safety with the bitartrate preparations. It is probable that drug fastness does occur, as has been suggested and if this is so intermittent therapy may again be of value.

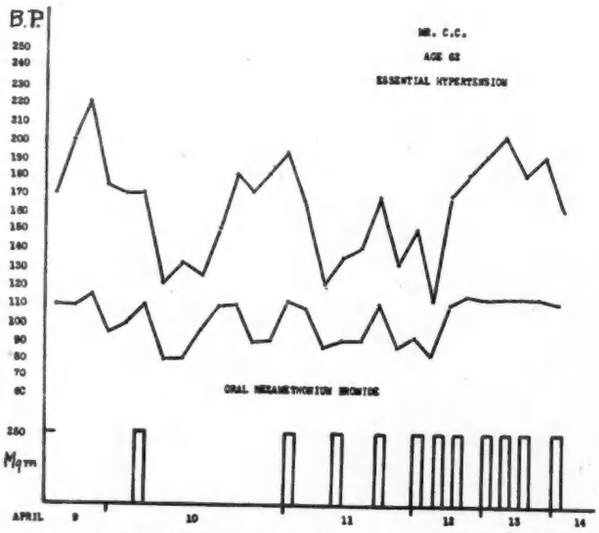

Fig. 4.—Blood pressure chart of a patient, male, aged 62 years, suffering from "essential hypertension". Note the extreme lability of the blood pressure following hospitalization and bed rest making the evaluation of the response to hexamethonium bromide extremely difficult.

Summary and Conclusions

The use of hexamethonium compounds in the treatment of 31 patients with hypertension is described.

The patients were divided into three groups and an attempt has been made to interpret the action of the compounds in each group. It is believed one may prophesy with some degree of accuracy the effect of the drug in the hypertensive patient, according to the group to which he belongs.

We believe that these compounds are capable of lowering the blood pressure temporarily in most hypertensive patients and feel that this drop, on the whole, is beneficial. Certainly all of our patients noted subjective improvement when their blood pressure fell. We do not feel that the sedative action of the bromide component in hexamethonium bromide can explain their subjective improvement as a similar result could be obtained with the bitartrate preparation. What part they will play in the long term therapy of hypertension is still to be discovered and it will take years of observation before their therapeutic rôle is determined.

It is felt that intermittent therapy may be more beneficial than continued therapy, as in some patients tolerance to the drug occurs.

All patients should be in hospital while the drug is being used for the first time, as vascular accidents may occur and cases of intestinal obstruction, due to the action of the drug, have been reported. If treatment is to be continued after leaving the hospital hexamethonium bitartrate should be used to avoid the possibility of bromide intoxication.

References

1. Paton, W. D. M. and Zaimis, E. J.: *Nature*, **161**: 718, 1948.
1a. Barlow, R. B. and Ing, H. R.: *Nature*, **161**: 718, 1948.
2. Paton, W. D. M. and Zaimis, E. J.: *Brit. J. Pharmacol.*, **4**: 381, 1949.
3. Organe, G., Paton, W. D. M. and Zaimis, E. J.: *Lancet*, **1**: 21, 1949.
4. Arnold, P. and Rosenheim, M. L.: *Lancet*, **2**: 321, 1949.
5. Burt, C. C. and Graham, A. J. P.: *Brit. M. J.*, **1**: 455, 1950.
6. Kay, A. W. and Smith, A. N.: *Brit. M. J.*, **1**: 460, 1950.
7. Restall, P. H. and Smirk, F. H.: *New Zealand M. J.*, **49**: 206, 1950.
8. Saville, S.: *Lancet*, **2**: 358, 1950.
9. Smirk, F. H.: *Lancet*, **2**: 477, 1950.
10. Campbell, A. and Robertson, E.: *Brit. M. J.*, **11**: 804, 1950.
11. Frankel, E.: *Lancet*, **1**: 408, 1951.
12. Paton, W. D. M. and Walker, J.: *Lancet*, **1**: 473, 1951.
13. Turner, R.: *Lancet*, **2**: 358, 1950.
14. Locket, S., Swann, P. G. and Grieve, W. S. M.: *Brit. M. J.*, **1**: 788, 1951.
15. Beckgaard, P.: *Acta. Med. Scandinav.*, Supp. **132**: 1946.
16. Watkinson, G. and Evans, G.: *Brit. M. J.*, **1**: 595, 1947.

"Cat-scratch Fever"—A New Clinical Entity.—A condition similar to, but much milder than, tularæmia, with fever, general malaise, symptoms of infection, and manifested by lymphadenopathy. It is acquired from cats, and is self-limited. The etiology is unknown and the treatment is symptomatic.—Greer, W. E. R.: *New England J. Med.*, **244**: 545, 1951.

THE SURGICAL TREATMENT OF MITRAL STENOSIS*

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THE surgery of great vessels for congenital heart disease lead naturally to a great deal of enthusiasm for intracardiac surgery, but while the former is a development of very recent years, it is interesting to note that attemps at dealing with stenosed mitral valves dates back to the beginning of the century.

Perhaps the earliest thoughts along these lines came with the discovery of the circulation by Harvey. Then in 1850 C. J. B. Williams described mitral valve disease and gave a very accurate description of the clinical murmurs and findings on which the diagnosis could be made clinically. A very acute observer, Samways in 1898, observed the rhythmic action in the heart of the horse. The organ was sufficiently large and had such a slow rate that he was able to see the rhythmic contraction of the auricle followed by that of the ventricle. His observation was probably the most important ever made in regard to the physiology of heart function. In 1902 Brunton[1] made a direct attack on the mitral valve, realizing its importance in obstruction in rheumatic heart disease and made an incision in this structure. In the following years, 1907 Cushing,[2] 1909 Bernheim,[3] 1912 Sheppelman,[4] 1922 Graham and Allen,[5] all had done a good deal of thinking and made some attempts at doing something about mitral stenosis.

It was evident from the writings of these surgeons that they were aware of the significance of the mitral valve and its importance in producing the symptoms of mitral stenosis. The most determined attack in trying to relieve mitral obstruction was made in 1924 by Cutler and Beck.[6] They succeeded in punching out portions of mitral valves with fairly good immediate results but the regurgitation seemed to be a greater handicap than was the pre-existing stenosis. For that reason they discontinued this work. In 1925 Souttar[7] dilated the mitral valve successfully. Then there appeared to be a lull in activity in this regard until in 1947 Smithy,[8] himself a sufferer from this disease, made a surgical attack on the mitral valve with considerable success. Since that time the work of Bailey, Glover and O'Neill,[9] Harken,[10] Blalock,[11] Potts,[12] Murray[13] have added a good deal of information to the surgical treatment of mitral stenosis.

My interest in the subject developed in the form of some experimental work in 1935, the results of which were published in 1938.[13] Lacking the support of my colleagues, or suffering from a faint heart, I did not apply this until 1945 when I operated upon my first patient. I am glad to say that that patient is still alive and working and does not seem to be failing in any sense, except from the inexorable march of time.

For the purposes of this paper, this subject might be considered under the headings that follow.

* The Mayo Foundation Lecture, delivered at The Mayo Clinic, Rochester, Minnesota, February 15, 1951.

WHAT IS THE DISEASE?

I shall mention only the fact that rheumatic infection, whatever may be its source, damages both the musculature as well as the valvular systems of the heart. It was thought in the time of McKenzie and Ross, as well as by many physicians in recent years, that the damage to the muscle was more important than the damage to the valves. Medical treatment, by and large, was therefore designed to improve the function of the muscle so that it might be more able to overcome the obstruction or the leaking of the valve systems. From my point of view, however, if there is increased work produced by stenosis or regurgitation at one or more valves, this adds an extra load to a muscle which is already damaged and, while the muscle can be improved in many respects, and the conduction changed to improve this function, if the heavy load imposed by obstructing valves could be relieved, then the muscle would be more able to carry on adequate circulation.

Added to these continuous difficulties, which usually increase until the circulation ultimately fails, there are complications which are responsible for death in a fair number of such patients. There is impaired circulation of the gastrointestinal tract and liver, causing a great deal of discomfort and contributing to a state of poor health probably from poor metabolism, also changes in the pulmonary vascular tree and lungs causing disability and attacks of asthma, pulmonary œdema and hæmorrhage.

The tendency to formation of thrombi in the left auricle, especially its appendix, and occasionally in massive form in the body of the auricle, may lead to embolism or, it is suggested, ultimately the presence of the obstructing thrombus in the auricle which embarrasses the circulation may suddenly obstruct the mitral valve. Post mortem evidence of death resulting from such sudden valvular obstruction from a thrombus, makes one wonder if some of the clinical episodes of sudden temporary failure of the circulation in such patients may not be the result of temporary blocking of such a nature, which fortuitously has relieved itself in time for survival. These points are mentioned because of their possible significance in relation to the criteria used for selection of patients suitable for surgical operation.

How Prevalent is the Disease?

In the United States, and I suppose our statistics in Canada, while not fully recorded, would follow closely those of that country, it is shown that rheumatic heart disease is the leading cause of death between ten and sixteen years of age. It is second only to T.B. between the ages of fifteen and twenty-four. Each year there are between six and seven hundred thousand deaths from heart disease and of these about two hundred and sixty-four thousand are rheumatic heart cases. A large number of these patients are in poor health and are semi or complete invalids and this is a giant economic problem. While one would hope that preventive medical measures eventually would prevent this disease, still for the present it leaves a great mass of material asking for improvement by surgery, medicine or any other means that can be provided. In favour of this disease responding to preventive medicine is the fact that it tends to occur mostly in poorer classes where there is over-crowding, and further evidence of this is the fact that 35 to 50% of patients have others with the same disease in the same family or in close relatives. Therefore, improvement of general conditions and nutrition might have a great deal to do in preventing this disease.

Effects and Course of the Disease

Statistically it is shown that about 50% of patients with mitral stenosis die in young life or middle age. The duration of life after developing mitral stenosis which is recognizable is about twenty years. When regurgitation is present, this period is considerably shorter. When considering surgical treatment, it is well to remember that after the first evidence of failure in a chronic case, the patient may live four to five years and after having an attack of hæmoptysis, which ordinarily is considered a late stage of the disease, the average duration of life is two to four years. Therefore, surgery, if it is to have a place in the treatment of this disease, must offer prospects better than those indicated.

The result of injury to the vascular system is of considerable interest to the surgeon. In about 85% of patients having rheumatic fever, there is evidence of valvular disease. In those in which the valves are involved, mitral stenosis alone occurs in about 50%. In another 19%, mitral stenosis is combined with aortic-valve lesions. Mitral aortic and tricuspid are involved in about 11% and the tricuspid in 3%, while the pulmonary is involved only in about 1% with mitral valve disease.

Symptoms will be considered only as they have a bearing on the selection of patients for or against operations. For the present at least, most patients with an established diagnosis of mitral stenosis are best treated medically. Surgery is indicated only if: (a) it is generally decided that the duration of life is likely to be shortened by the disease and that surgery has a prospect of prolonging this; (b) the patient's disability is sufficient to justify an operation and that surgery has a fair prospect of reducing the disability; (c) the complications may be prevented or diminished by operation.

The decision on these problems falls to the lot of the physician and every available form of investigation must be called into use to help make the decision. It has been my policy to operate only on patients who have: (a) Unequivocal signs of mitral stenosis. (b) No valves other than the mitral involved, or, if so, only to a very slight degree. (c) There must be no active heart infection present. (d) The rheumatic fever must be in a quiescent stage. (e) Progressive failure and increasing disability in spite of medical treatment.

All the patients on whom I have operated have been under medical treatment and in spite of this, they have shown signs of failure. There has been dyspnœa, usually at rest, and always on exertion. In some orthopnœa, occasionally pulmonary œdema; some have had hæmoptysis; a varying amount of cyanosis with distension of neck veins in some, with enlargement of liver, œdema, ascites and an enlarged heart. All but 4 of 37 patients operated upon have had auricular fibrillation. Various clinical, x-ray and laboratory tests to establish the diagnosis and estimate the stage of the disease have been carried out. In spite of all the evidence obtained by investigation, I have found from my experience at operation that there are some other hazards which are very perplexing. I feel the answer to these must be found before a satisfactory decision can be made as to whether a patient is suitable for operation or not.

The first is the problem of massive thrombosis in the left auricle. This has been a major factor in deciding whether something could be accomplished at operation or not. In 8 patients, other than the 37 named as patients operated

upon, a massive thrombus was found in the left auricle on exploration.[14] This thrombus involved the left auricular appendage and formed a mass within the auricle the size of one's fist or considerably larger and in one patient the thrombus extended right through and could be followed well out in the upper pulmonary vein on the left side. In one such patient, the thrombus was probably the size of one's fist, but there seemed to be a fair amount of auricular wall which was flexible and it was thought one might take a chance and divide the mitral valve, taking as great care as possible not to disturb this thrombus. The instrument was passed through the valve without difficulty and was felt in the auricle by depressing the flexible portion of the wall, then a good incision was made through the valve. The patient seemed to be considerably benefited immediately by this and we were quite pleased with his condition on return to the ward. However, within twenty-four hours, it was evident that he had a massive embolism at the bifurcation of the aorta.[15] With his recent heart operation and his general poor condition with this embolism, I was afraid to do anything further and he succumbed. Obviously I should not have done anything to the mitral valve. In the other seven on making this diagnosis. I closed the chest without doing anything further.

My great problem, therefore, is to determine clinically beforehand whether there is a thrombus in the left auricle or not. To my mind, this is one of the heavy and difficult problems. On going over these patients very carefully, I have come to the conclusion that a massive thrombus of this sort is to be expected if: (a) there is a doubtful looking shadow, added to the heart shadow, which might be interpreted as lying in the region of the left auricle; (b) if a patient has been doing fairly well but finally gets to a stage where there is relatively little response to all forms of treatment and the general condition seems to be sagging with increasing failure in spite of treatment and rest. While this might be the result of other features, it has been a factor which has been constant in this group; (3) calcium in the wall of the auricle.

We have tried to do angiocardiograms, but so far the results have not been very satisfactory. I saw one patient in Rio de Janeiro recently in whose x-ray there was a shadow which, I think, fairly certainly, might have been interpreted as a thrombus in the left auricle. However, as the patient was not operated upon, one cannot prove that such was the case. He was thin of stature and the heart shadow stood out in great contrast to the lighter surrounding somatic structures.

The second problem which must be determined beforehand, if possible, is the question of permanent vascular changes in the pulmonary vascular tree and in the lung tissue. Unfortunately, two of my fatal results following operation were in patients in whom there was no improvement following division of the mitral valve, who at post mortem were shown to have basement membrane thickening of the pulmonary capillaries, and arteriosclerotic changes in smaller and larger pulmonary artery vessels in the lung. Recent articles by Welsh, Johnston,[10] Larrabee, Parker and Edwards[17] here, also Parker and Weiss,[18] describe these conditions and there is an awareness about this lesion. It appears to be irreversible and I would consider it an absolute contraindication to operation. These studies have been on pathological material, as have been mine, and this does not help in identifying it preoperatively. Not long ago I was congratulated by the pathologist on providing them with such a case following operation, but I must say that gave me little satisfaction, because I want to know before making the decision to operate. The only positive information which may suggest such a lesion, and it is not an unequivocal finding, is marked pulmonary hypertension. All the patients on whom I have operated have had pulmonary hypertension, but it is alleged that if the pulmonary pressure goes above 100 millimetres of mercury on catheterization, this is a contraindication. So far as I know to date, this is the best warning of the presence of such vascular changes in the lung and if established is a contraindication to operation.

By and large, the patients who are likely to benefit from operation are those in whom medical treatment has failed, and who are unable to carry on, on this account. On the other hand, I have operated on a few patients who were in late or final stages of heart failure with enormously enlarged hearts who have benefited temporarily, but I think the results have not been worth while. There is a group, therefore, at the farther end of the course of heart disease, who, for the present at least, are not suitable, or do not stand to benefit by surgical treatment, and should not be operated upon.

SURGICAL TREATMENT

I shall mention only the question of relieving pulmonary hypertension by producing interatrial septal defects, as suggested by Blalock,[19] Bailey,[20] and the anastomosis of the pulmonary to azygos vein, as suggested by Sweet,[21] which methods have given improvement in groups of patients. There is also the possibility of relieving some of the symptoms of heart disease by attacking the nerve supply, but that does not come within the scope of this paper.

The other possible surgical procedures are: (1) Direct approach, when the valve is divided. (2) Resection of a portion of the stenosed valve. (3) Resection of a portion of the valve and replacement by a new valve. (4) Short circuiting of the stenosed mitral area by various methods, where either vein grafts or the auricular appendage has been used to produce a bypass from the auricle or pulmonary veins to the left ventricle (Rapaport[22]).

The possible approach for dealing with the mitral valve directly may be either through the left auricle or the left ventricle. You are all familiar with the successful work of the late Smithy,[8] of Bailey, Glover, O'Neill,[9], Harken,[10] Brock[23] in London, and many others. One must decide, therefore, on the approach to be used, and just what is to be attempted on the valve itself. In some of my earlier patients, the operation was carried out through the left auricle, but my preference at the present time is for an approach through the left ventricle. The incision for the anterior approach is rather a large dissection. However, the patient tolerates this very well and the time involved is not great. I have completed several of these operations within an hour and the average time is within an hour and a half. On all occasions, some of this time is spent in watching the heart action and demonstrating the effect as well as in taking measurements, etc.

I make the large exposure, turning back a flap of the chest wall, and open the pericardium widely because it gives a picture of the condition of the heart as a whole, which is not available through a smaller approach to the left auricle. This approach exposes both right and left auricles and right and left ventricles and it is my custom, if things are going well, to get manometric pressure readings from the pulmonary artery and both auricles on the operating table before and after the valve has been attacked. I am always greatly impressed with the great rotation of the heart to the left, bringing the right ventricle entirely to the front and sometimes the left ventricle does not appear at all on the anterior surface. The next feature is the tremendous enlargement of the right auricle. If an approach is made through the left auricle, this is not seen, and my medical colleagues have criticized me for comments regarding the enlargement of the right auricle. However, there is no question about the tremendous distension of this chamber in the patients on whom I have operated.

With intravenous novocaine running, with positive ventilation anæsthesia and with some novocaine in the pericardial sac, we have been able on practically all occasions to carry out what we have designed to do. While I have exposed many others,[24] I have operated upon 37 mitral valves and what I am relating now is the result of this experience. There have been no deaths on the operating room table. Only one of these patients has been transfused, before, during or after the operation.

With novocaine injected at the site of entering the left ventricle, there are some extra systoles, but there has been very little concern regarding failing heart action during this procedure. In two patients, ventricular fibrillation occurred. In one the manipulation within the left ventricle had been too vigorous and too prolonged. In both of these, we were able by cardiac massage to restore normal rhythm. One of these patients, on whom I operated about a year ago was in to see me a few weeks ago, and from being an in-and-out-of-bed invalid, she now is doing her own work. She came to see me because one of the wires with which we had tied the sternum together was rubbing underneath the skin and was bothering her when she was bending over the washing board doing the family washing. One firm push with the thumb bent the wire down out of its prominent position and the patient returned to her washing.

The remainder of the work comes down to a matter of gadgets. The instruments of several operators are beautiful specimens. Still, what I use, with no special preference, is my own home made variety with which I am able to accomplish this work fairly satisfactorily.

It consists of a cannula with a valve, much as in a cytoscope, through which the instrument can be passed. Either a scissors or a punch can be used to take out portions of the valve.

A cardioscope[25] has been devised with which one can see something of what goes on inside. In most of the patients I have, with the scissors, divided the valves to produce the commissurotomy effect. The results of this are excellent in some, as shown by the pressures in the left auricle, right auricle and pulmonary artery before and after division of the valves.

My best results have been in a small group in whom I have removed a large portion of the rough, scarred, stenosed valve and replaced this with a new valve. Originally I thought that the more of this valve that could be removed, the better, but as Cutler[6] showed, this produces regurgitation. It seemed that this rigid scarred valve would be better removed and replaced by more flexible material, which would provide the ideal result, and such has been the case in the small group in which it has been used. It has not been applied in all cases because of the greatly enlarged hearts, and the more operating required. Therefore, I thought it justifiable to do the lesser procedure in most, to observe the results and to have a fair proportion of survivals.

If, however, a portion of the valve has been resected or punched out, then I think it is a necessity to put in a new valve. This has been accomplished by using material which is flexible, strong, will not produce clotting or thrombosis, will not wear out and will live and get its nourishment from the blood stream. For these requirements, a sufficient length of cephalic vein has been removed, turned inside out, and through the lumen has been passed a tendon of palmaris longus. This has been suspended between the front and back walls of the heart in such a way that on systole it blows into the defect produced in the mitral valve. It is placed sufficiently on the ventricular side that it floats freely out of the opening and does not prevent ventricular filling on diastole.[24] One such valve, working in an animal's heart for seven years, appears to be in good condition, and has worn well without signs of degeneration or deterioration. While I have operated on 37 valves, I have explored eight others in whom there was massive thrombus in the left auricle on which nothing was done. Then there was another group of about twenty in whom an anæsthetic was given and under a period of observation we were not satisfied with the general condition of the patient. The cyanosis did not improve with oxygen. The blood pressure went down to sixty or seventy and did not return, or the neck veins became more distended and tense, and the heart rate accelerated, then we discontinued the anæsthetic and nothing further was done.

RESULTS OF SURGICAL TREATMENT

Of 37 valves operated upon, the hospital mortality rate has been about 20%. The first patient operated upon, now going in his sixth year with a resected valve replaced by a new valve, is doing well and is fairly energetic. Fifty-five per cent of all operated upon have what might be termed fairly good results, with ability to return to some sort of work. One man, for example, who was a semi-bed invalid, has now returned as a brakeman on a train and has been at this job for about a year and a half. He has no failure, is losing no time and his condition is excellent throughout. Several of the women are doing their own housework and are very happy with their improved health. Another 25% are improved and go back to work and do fairly well for a time, but within a period of from four to six months, many have relapsed into failure and many of these have died. The remaining 20%, have survived operation but within a matter of a few hours or a few days, have increasing difficulty and have not survived. In this group have been those with massive auricular thrombi and some have been shown to have irreversible changes in the pulmonary tree.

While there is great enthusiasm at present over the future of surgical treatment for this disease, I think this must be tempered with great caution. I am sure some patients are much improved, still the difficulty seems to be in the proper selection of the right cases. The situation is much the same as it was in respect to congenital heart disease[26] when, with the advent of surgery, it became necessary for the physician to separate and distinguish the various types of the disease so that those suitable for surgery might be selected. The problem is similar in mitral disease and if the proper patients can be selected, then surgical treatment offers them considerable improvement, for the present at least. One does not know how long these results will last, nor whether the disease will reactivate and heal up the incisions made in valves, or what the end result may be. My own efforts have been slowed down somewhat and the problem approached more cautiously because of the pos-

sibility of some day having a method of direct approach to these valves which would eliminate these indirect methods. If such should be the case, then these methods will become obsolete over night.

REFERENCES

1. BRUNTON, SIR L.: *Lancet*, 1: 352, 1902.
2. CUSHING, H. AND BRANCH, J. R. B.: *J. Med. Res.*, 12: 471, 1907-1908.
3. BERNHEIM, B. M.: *Bull. Johns Hopkins Hosp.*, 20: 107, 1909.
4. SCHEPPELMANN, E.: *Arch. f. Klin. Chir. Berl.*, 97: 739, 1912.
5. ALLEN, D. S. AND GRAHAM, E. S.: *J. A. M. A.*, 79: 1028, 1922.
6. CUTLER, E., LEVINE, S. AND BECK, C.: *Arch. Surg.*, 9: 689, 1924.
7. SOUTTAR, P. W.: *Brit. M. J.*, 2: 603, 1925.
8. SMITHY, H. G.: Annual Assembly of the Southeastern Surgical Congress, April 5 to 8, Hollywood, Fla., 1948.
9. BAILEY, C. P., GLOVER, R. P. AND O'NEILL, T. J. E.: *J. Thoracic Surg.*, 19: 16, 1950.
10. HARKEN, D. E.: *J. Thoracic Surg.*, 11: 656, 1942.
11. BLALOCK, A. AND TAUSSIG, H. B.: *J. A. M. A.*, 128: 189, 1945.
12. POTTS, W. J., SMITH, S. AND GIBSON, S.: *J. A. M. A.*, 132: 627, 1946.
13. MURRAY, G., WILKINSON, F. R. AND MACKENZIE, R.: *Canad. M. A. J.*, 38: 317, 1938.
14. MURRAY, G.: *Brit. J. Surg.*, 27: January, 1940.
15. *Idem*: *Surg. Gynec. & Obst.*, 77: 157, 1943.
16. WELCH, K. J., JOHNSON, J. AND ZINSSER, H.: *Ann. Surg.*, 132: December, 1950.
17. LARRABEE, W., PARKER, R. EDWARDS, J.: *Proc. Staff Meet. Mayo Clin.*, 24: 316, 1949.
18. PARKER, F. AND WEISS, S.: *Am. J. Path.*, 12: 573, 1936.
19. BLALOCK, A. AND PARK, E. A.: *Ann. Surg.*, 119: 445, 1944.
20. BAILEY, C. P.: *Dis. of Chest*, 15: 377, 1949.
21. SWEET, R. H. AND BLAND, E. F.: *Ann. Surg.*, 130: 384, 1949.
22. RAPPAPORT, A. M. AND SCOTT, A. C.: *Ann. Surg.*, 131: 449, 1950.
23. BROCK, R. C.: *Brit. M. J.*, 1: 1121, 1948.
24. MURRAY, G.: *Arch. Surg.*, 61: 903, 1950.
25. *Idem*: *Angiology*, 1: August, 1950.
26. *Idem*: *Brit. M. J.*, 2: 905, 1947.

RÉSUMÉ

La plupart des malades souffrant de sténose mitrale s'accomodent mieux actuellement du traitement médical de cette affection. La chirurgie n'est indiquée que si l'on peut être raisonnablement sûr: a) de prolonger la vie du malade, b) de diminuer son degré d'impotence, c) de prévenir les complications de la maladie.

L'auteur dit ne devoir opérer que les malades chez lesquels les signes de sténose mitrale sont nettement établie et les autres valves en bon état. En outre le cœur ne doit pas être le siège d'une infection en activité ou de rhumatisme articulaire. Tous ses malades, d'ailleurs, avaient déjà été traités médicalement et montraient de l'insuffisance cardiaque à certains degrés.

Avant d'opérer, deux précautions sont indispensables, à savoir s'assurer qu'il n'existe pas de thrombose massive dans l'oreillette gauche, ni de signes de changements vasculaires permanents dans la circulation pulmonaire, qui se traduisent ordinairement par une hypertension pulmonaire.

Après s'être étendu sur la technique opératoire, l'auteur discute sur les résultats obtenus: 20% de mortalité opératoire, 55% d'assez bons résultats avec reprise d'une activité à peu près normale, et 25% dont les bons résultats ne se maintiennent que pour un certain temps. En somme, il importe avant toute opération de ce genre de pratiquer une sélection rigoureuse des cas qui conviennent.

THE TREATMENT OF PEPTIC ULCER IN GENERAL PRACTICE*

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APPROXIMATELY 5 to 10% of the people of this country will develop a peptic ulcer during a lifetime.[1] Thus the diagnosis and treatment of this disease is of major importance to the practising physician.

This paper is devoted to the handling of the uncomplicated ulcer as it is met in the everyday practice of medicine. This includes both treatment of the acute attack and the prevention of recurrences. Reference will be made only to those complications which are treated medically or where the decision must be made between medical and surgical treatment.

The management of the uncomplicated gastric and duodenal ulcer consists of: first, the treatment of the acute attack, and second the prevention of a recurrence of the ulcer.

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TREATMENT OF THE ACUTE ATTACK

In managing the acute attack, rest, diet and the reduction of gastric acidity form the framework of treatment.

BED REST

The length of bed rest will depend on three factors: (1) the severity and duration of the symptoms, (2) the patient's economic status, and (3) his mental attitude. Normally, bed rest is enforced until the patient is completely free of symptoms. Then follows a convalescent period of a week or two. Sedatives should be used freely to assist in the promotion of rest. Where economic or other factors make absolute confinement in bed impossible, one may be forced to follow an ambulatory regimen. Only patients with the mildest symptoms should be treated in this way.

DIET

During the acute phase the diet should consist of hourly feedings of a three ounce mixture of equal parts of milk and cream. On this regimen, most patients with uncomplicated ulcer will lose their symptoms within a few days. When the acute symptoms have subsided, three bland meals, chosen from the food listed

TABLE I.

FOODS TO BE TAKEN IMMEDIATELY FOLLOWING THE ACUTE SYMPTOMS

Milk and cream	Macaroni
Eggs (not fried)	Spaghetti
Cooked cereals	Squash, carrots, spinach, beets, peas—all puréed
Cream soups	
Meats (well cooked and ground)	White bread (not fresh)
Fish (not fried or oily)	Butter or oleomargarine
Chicken	Gelatin products
Potatoes (mashed or baked)	Cream or cottage cheese

TABLE II.

FOODS WHICH MAY BE ADDED AFTER THE FIRST MONTH OF TREATMENT

Meats (all kinds, except those which are fibrous, tough or spicy; no fried meat)	Cauliflower
	Vegetables in Table I, without puréeing.
Potato (any form except fried)	Orange juice or grapefruit juice (after breakfast)
	Ice cream
String beans	Soft puddings
Asparagus	Stewed fruit

in Table I, may be superimposed on the basal hourly feedings of milk and cream.

When the patient is ready to return to work, the diet may be increased to include the foods listed in Table II. The following should be avoided at all times: fried or "greasy" food; condiments, alcohol, caffeine beverages, "pop"; rough or fibrous foods; pies, pastry, candy; any food which has previously caused the patient distress.

Hourly feedings should be continued but the patient may alternate the milk and cream mixture with an antacid.

Thus, when the patient is ready to return to work, his day's routine would be approximately as follows: 8.00 a.m., breakfast; 9.00 a.m., mineral antacid; 10.00 a.m., milk and cream; 11.00 a.m., mineral antacid; 12.00 noon, lunch; 1.00 p.m., mineral antacid; 2.00 p.m., milk and cream; 3.00 p.m. mineral antacid; 4.00 p.m., milk and cream; 5.00 p.m., mineral antacid; 6.00 p.m., supper; 7.00 p.m., mineral antacid; 8.00 p.m., milk and cream; 9.00 p.m., mineral antacid; 10.00 p.m., bedtime—milk and cream plus antacid.

REDUCTION OF GASTRIC ACIDITY

In an attempt to neutralize gastric acid, some physicians advise their patients to take feedings in the mid-morning, mid-afternoon and evening, or even feedings every two hours. It will be seen in Fig. 1 that such a regimen has little neutralizing value. However, the hourly feeding of milk and cream previously mentioned, combined with a mineral antacid, produce good neutralizing action (Fig. 2). If an inhibiting antacid is added, excellent inhibition of acid production occurs.

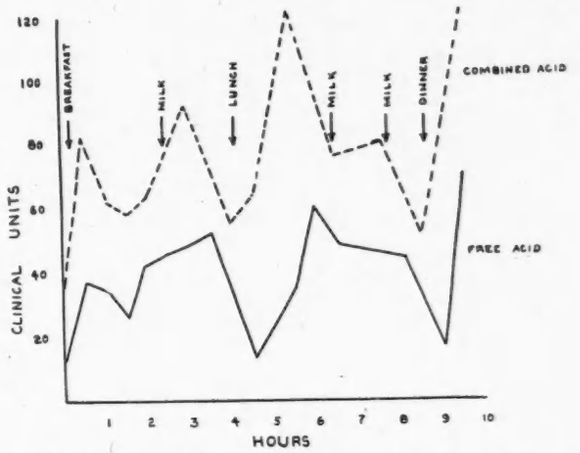

Fig. 1.—The minimal effect on gastric acidity of two hourly feedings.

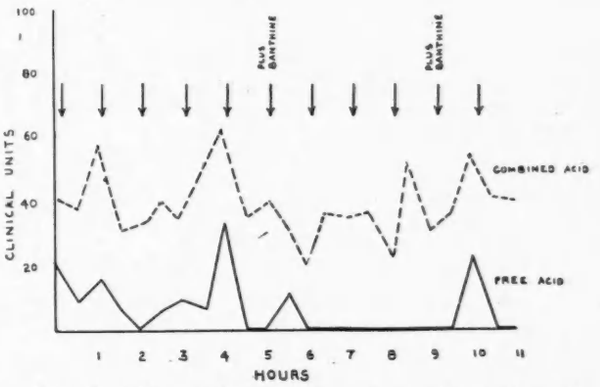

Fig. 2.—The good reduction of gastric acidity obtained by hourly feedings of milk and cream combined with an antacid (calcium and magnesium carbonate). The addition of banthine produced complete inhibition of gastric secretion. The rise of acid at the 4 hour and 10 hour periods represent psychic secretion of acid when the subject observed other patients eating lunch and supper.

According to their physiological action, antacids may be divided into two groups. Those in the first group include mineral antacids, gastric mucin, protein hydrolysates, and anion exchange resins. These neutralize acid. The second group consists of parasympathetic blocking agents and certain hormonal preparations. These inhibit acid production.

Mineral antacids are of two types. The first includes sodium bicarbonate, calcium carbonate, magnesium carbonate, and oxide, which act through a chemical reaction with the acid. Antacids of the second type react very slowly with the acid, and their chief action is adsorption of hydrochloric acid. Magnesium phos-

phate, magnesium trisilicate, and aluminum hydroxide are thus called colloidal or non-reactive antacids.

Gastric mucin has been used in the belief that it protects gastric mucosa. In animals it is of value in the prevention of experimental peptic ulcer. Clinical trials have not been too impressive, but it does seem to help an occasional resistant case.[2, 3, 4]

Protein hydrolysates and triple strength powdered milk are effective neutralizers of acid, whereas whole milk has little effect. The addition of protein hydrolysates or powdered milk to the whole milk of the diet has the beneficial effect of increasing the protein value of the diet as well as the neutralizing value.

The use of *anion exchange resins* has recently attracted much interest.[5] These act by adsorbing acid in the stomach and subsequently releasing it lower down in the intestine. In comparable dosage, the clinical effect of exchange resins seems about the same as aluminum hydroxide gel.[6]

The inhibiting effect of atropine on gastric secretion and motility is well known. Another atropine-like compound, banthine, is receiving wide publicity. Its action is similar to atropine in blocking the vagal nerve impulses. Unlike atropine, sympathetic nerve impulses are blocked as well. Claims have been made that it is less toxic than atropine and its action of longer duration, but experimental evidence does not bear this out.[7]

The work of Ewald in 1896 showed that fat in the duodenum inhibits gastric secretion and motility. The mechanism of this action by fat is through the production of a hormone, enterogastrone, in the upper small bowel mucosa. This hormone is carried through the bloodstream to the stomach, where it exerts its inhibiting action on the gastric glands. Part of the effectiveness of the original Sippy milk and cream regimen was due to the fat in the cream which, on reaching the duodenum, stimulated the production of enterogastrone. Some clinicians actually administer fat to reduce acidity. Recently the active hormone, enterogastrone, has been extracted from the mucosa of the upper small intestine and used in the treatment of ulcer.[8]

Urogastrone is a hormonal substance obtained from the urine and may well prove of therapeutic value. Another urinary substance, uroanthelone, is in clinical use. It does not inhibit gastric secretion, and its mechanism of action is believed to be through the promotion of fibroblastic and epithelial healing of the ulcer.[9, 10, 11]

PREVENTION OF RECURRENCES

"All evidence points to the fact that ulcer is a chronic disease and that all present methods of treatment are merely palliative."[12] This pessimistic statement was made by Emery and Monroe in 1929 and is true today. The graph in Fig. 3 indicates that this is the experience of most authorities. The prevention of recurrence is more difficult than the treatment of the acute attack.

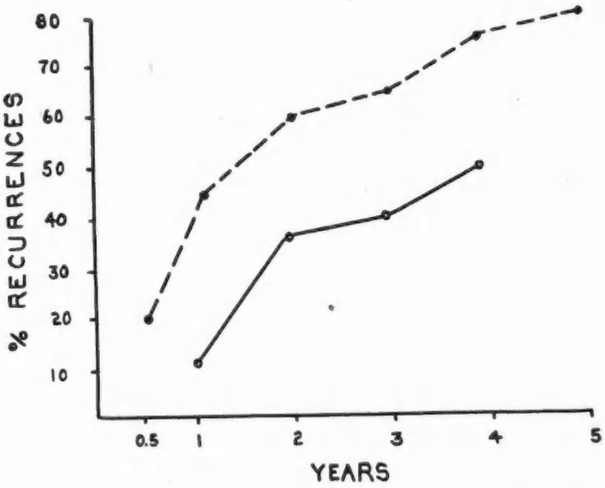

Fig. 3.—Broken line. Showing curve of recurrence of ulcer. Solid line. Showing curve of recurrence if patients who are improved, though having had a recurrence, are subtracted. For example, 90% of patients at one year are symptom free or improved.

If most ulcer patients suffer a recurrence of symptoms despite therapy, is there any value in adhering to a diet? A comparison between treated and non-treated cases is shown in Table III. Over an average period of 3 to 9 years 81% of treated cases improved, whereas only 49% of untreated cases improved.

If, then, adherence to a diet is of value, how strict should the diet be? Again Emery and Monroe provide figures showing that patients on a strict diet maintain better health. The figures in Table IV indicate that a statistically higher percentage of patients without symptoms is found in the group on a complete Sippy regimen.

Surgical intervention appears no better than medical treatment in altering the course of the uncomplicated peptic ulcer. Table V compares the results of medical and surgical treatment in comparable groups of patients who had un-

TABLE III.

COMPARISON BETWEEN TREATED AND UNTREATED PATIENTS WITH PEPTIC ULCER

	Treated patients		*Untreated patients*	
	No. of patients	*Percentage*	*No. of patients*	*Percentage*
No symptoms...	221	17.5	30	23.8
Very few symptoms..	411	32.6	11	8.7
Definite improvement	389	30.9	20	15.8
Improvement...	65	5.1	5	3.9
No improvement	172	13.6	60	47.6
	1,258		126	

From Emery and Monroe.[12]

TABLE IV.

COMPARISON BETWEEN VARIOUS DIETS IN PATIENTS WITH PEPTIC ULCER

	5 meals, alkaline powders Percentage	*Partial Sippy Percentage*	*Complete Sippy Percentage*
No symptoms.....	13.1	13.4	25.0
Very few symptoms....	36.7	38.2	31.0
Definite improvement.	30.3	33.5	34.4
Improvement.....	6.4	6.7	5.1
No improvement..	13.3	7.8	5.1

From Emery and Monroe.[12]

TABLE V.

RESULTS OF 426 MEDICAL AND 90 SURGICAL TREATMENTS IN PATIENTS WITH PEPTIC ULCER WITHOUT COMPLICATIONS

	Medical cases		*Surgical cases*	
	No. of cases	*Percentage*	*No. of cases*	*Percentage*
No symptoms.....	86	20.1	24	26.4
Very few symptoms....	184	43.1	18	20.0
Definitely improved.....	112	26.3	22	24.4
Improved.....	15	3.5	10	11.1
Unimproved....	29	6.8	16	17.7
	426		90	

From Emery and Monroe.[12]

complicated peptic ulcers. Some physicians regard surgical treatment as a curative one. They do not insist that the patient follow a strict and prolonged ulcer regimen following the operation. This may explain why the recurrence rate of ulcer symptoms in patients who have had surgical therapy is about the same as that of medically treated patients.

The figures presented would indicate that the best hope of avoiding recurrences is adherence to a strict ulcer regimen. It is difficult for most patients to take hourly feedings of milk and cream at work. However, most patients can take hourly feedings if the milk and cream, or milk alone, is alternated with antacid. At gatherings where it is difficult to take either milk or antacid the patient may be tided over by slipping an amphojel tablet in his mouth at hourly intervals. The foods listed in Table II permit the patient three fairly liberal meals.

A most important factor in the prevention of recurrences is the education of the patient. This education should start on the patient's first visit. He should be told about his disease and what he should do to remain well. The natural history of peptic ulcer, the importance of acid, and measures to combat this acid, should all be explained. The necessity of following a program of a restricted diet and frequent feedings for many years must be impressed on the patient.

The patient should be instructed in the importance of eliminating emotional strain. However, elimination is rarely possible, and he must then take measures to minimize the effect of emotional strain. Alvarez[14] wisely makes the following recommendation: "When a patient who has had an ulcer goes through an emotional crisis, he should immediately start taking food every hour or two. He shouldn't wait for the expected flare-up or hæmorrhage or perforation". To this excellent advice might be added the recommendation the patient goes to bed as soon as he returns from work, that he follow the most rigid ulcer regimen, that is, hourly feedings of milk and cream, combined with an antacid, and that sedatives be liberally used. A day or two of this prophylactic routine may prevent a month of curative therapy if the ulcer reactivates.

While there is no proof in the literature that smoking increases gastric secretion or motility, on clinical grounds the patient should try to stop smoking.[15] As both alcohol and caffeine stimulate gastric secretion, they should be prohibited.

Recently enterogastrone and radiation therapy have been employed to reduce the recurrence rate. Enterogastrone, the duodenal hormone, appears to be effective, but at present must be injected several times weekly, and therefore is not practicable.[8] Radiation therapy to the gastric area is used by Chicago workers to produce hypo- or anacidity. They report the recurrence rate of ulcers has been reduced 50% by this means.[16]

MANAGEMENT OF HÆMORRHAGE

About 25% of peptic ulcer patients hæmorrhage at some time, but only 5% of these bleeding patients die from the hæmorrhage. This figure rises to 30% in older patients with massive bleeding.

The basic treatment of bleeding peptic ulcer is, essentially, administration of adequate amounts of whole blood. This may mean several thousand cubic centimetres of blood. There is a tendency to underestimate the amount of blood to be given. Morphine is not recommended, because of the danger of producing vomiting, and the general absence of pain. Sodium phenobarbital, grains 2 intramuscularly, is an excellent sedative.

A bleeding patient is usually anorexic and there is little justification for forcing food. Free blood in the stomach cavity is, in itself, an excellent antacid. Because of the anorexia there is little gasric peristalisis and secretion. Within a few hours of cessation of bleeding, most patients will wish for food. Appetite returns with gastric peristalsis and gastric secretion. They should then be started on the strict ulcer regimen already described. Iron in the form of ferrous gluconate, grains 15 daily is added in a few days.

The high mortality rate in the older age group suggests that, for these patients, transfusion alone is not always successful therapy. Table VI

TABLE VI.

MASSIVE UPPER GASTROINTESTINAL HEMORRHAGE IN PATIENTS OVER 45 YEARS OF AGE BETWEEN 1943 AND 1949 AT THE TORONTO WESTERN HOSPITAL*

	Survived	*Died*
Duodenal ulcer	17	1
Gastric ulcer	2	11
Peptic ulcer (suspected)	9	3
No diagnosis	6	4
Carcinoma stomach	3	1
Cirrhosis of liver	2	—
	39	20

*Massive hæmorrhage is one of sufficient severity to produce definite clinical shock.

demonstrates the poor results at the Toronto Western Hospital of purely medical treatment of massive hæmorrhage in older patients. In an attempt to improve this figure, selected older patients with massive bleeding are being submitted to emergency surgery and the results compared with a control group of medically treated cases. The selection of patients for the surgical group is made as follows.

Generally speaking, all patients are treated medically except those over the age of 45 who have massive hæmorrhage. Older patients, with massive or recurrent bleeding, are carefully screened to decide which would benefit by emergency surgery. Four criteria must be fulfilled before surgery is recommended: (1) Patient over the age of 45 and suffering from massive hæmorrhage; (2) Bleeding not stopping under medical treatment or recurring after once stopping; (3) Source of bleeding known; (4) Surgery can be performed within 48 hours of bleeding.

In order to establish an early diagnosis, two special techniques are employed. The first is a radiological examination of the stomach, which is performed as soon as shock is counteracted. The second is a bromsulphthalein dye test of liver function. This particular test of liver function is of value, as the result is not altered by hæmorrhage.[17] A normal bromsulphthalein test rules out cirrhosis of the liver and œsophageal varices as the source of the bleeding. The occasional case of hæmorrhage from œsophageal varices of Banti's syndrome will not be detected by the bromsulphthalein test. However, these patients are usually under the age of 45 years and therefore not considered for surgery.

As Finsterer has pointed out,[18] the surgical mortality rises from 5 to 30% if operation is performed after 48 hours of bleeding. Hence the necessity of performing surgery early or not at all. The practice of permitting an older patient to bleed for several days and then finally submitting him to surgery is to be deprecated.

MANAGEMENT OF GASTRIC ULCER

Whether malignant degeneration is a complication of benign ulcer is an unsettled question. Therefore, to differentiate between a benign or malignant gastric lesion is a most important, and often a most difficult, problem. The obviously ulcerating carcinoma, the polypoid lesion which protrudes into the lumen of the stomach, and the diffusely infiltrating lesion, are all manifestly malignant lesions. It is the ordinary benign-appearing "punched out" gastric ulcer which presents a diagnostic problem, because almost 10% of these apparently benign ulcers will prove to be malignant.[19, 20]

Ulcers along the greater curvature and fundus have a slightly higher incidence of malignancy than elsewhere, otherwise the site of the ulcer is of little value in the differential

diagnosis. Prepyloric ulcers have no higher incidence of malignancy than lesser curvature ulcers.[19, 20, 21]

The clinical history of the patient, the size of the ulcer, and the level of gastric acid, are of no assistance in differentiation. However, the absence of free hydrochloric acid after histamine stimulation is very strong evidence that the ulcer is malignant.[19, 20]

If the radiologist with all his technical accuracy, the surgeon at operation, and the pathologist holding the gross specimen in his hand, cannot differentiate the benign from the malignant gastric ulcer, how will the physician differentiate? Just as a positive Wassermann forces the physician to diagnose syphilis until proven otherwise, so the radiological report of a benign gastric ulcer forces the physician to regard it as malignant until proved otherwise.

Proof consists of complete healing of the ulcer and continuing of healing as evidenced by radiological disappearance of the ulcer, freedom from symptoms, and absence of occult blood in the stool. It is imperative that the patient be followed for one year at least. During this time he should be carefully checked at the three months, six months, and one-year periods. A recurrence of his ulcer is an indication for surgery.

SUMMARY

The treatment of the acute attack of gastric and duodenal ulcer consists of bed rest and hourly feedings of a mixture of milk and cream. Later, three bland meals are superimposed on the basal hourly feedings. When the patient returns to work, a more liberal diet is permitted and a mineral antacid may be alternated with the basal hourly milk and cream. The various types of antacids, including the newer inhibiting and hormonal antacids, have been outlined.

Measures to minimize the possibility of ulcer recurrence have been discussed.

The administration of adequate amounts of whole blood is the most important therapeutic measure in the treatment of the hæmorrhaging peptic ulcer. Emergency surgery may be lifesaving for the occasional older patient with massive bleeding. The selection of such cases for surgery has been discussed.

The benign-appearing gastric ulcer may be a "wolf in sheep's clothing". Such a lesion must be regarded as malignant until proved otherwise. Proof consists of complete healing, and maintenance of healing, as evidenced by radiological disappearance of the ulcer, freedom from symptoms and absence of occult blood in the stool.

REFERENCES

1. IVY, A. C., GROSSMAN, M. I. AND BACHRACH, W. H.: Peptic Ulcer, The Blakiston Company, Philadelphia, p. 651, 1950.
2. KIM, M. S. AND IVY, A. C.: *J. A. M. A.*, **97**: 1511, 1931.
3. ATKINSON, A. J.: *J. A. M. A.*, **98**: 1153, 1932.
4. BROWN, C. F., CROMER, S. P., JENKINSON, E. L. AND GILBERT, N. C.: *J. A. M. A.*, **99**: 98, 1932.
5. MARTIN, G. J. AND WILKINSON, J.: *Gastroenterology*, **6**: 315, 1946.
6. WIRTS, C. W., SULLIVAN, B. H. AND HEMMERLY, W. C.: *Gastroenterology*, **15**: 1, 1950.
7. BENJAMIN, F. B., ROSIERE, C. E. AND GROSSMAN, M. I.: *Gastroenterology*, **15**: 727, 1950.
8. CREENGARD, H., ATKINSON, A. J., GROSSMAN, M. I. AND IVY, A. C.: *Gastroenterology*, **7**: 625, 1946.
9. PAGE, R. C. AND HEFFNER, R. R.: *Gastroenterology*, **11**: 842, 1948.
10. SANDWEISS, D. J., SALTZSTEIN, H. C., SCHEINBERG, S. R. AND PARKS, A.: *J. A. M. A.*, **144**: 1436, 1950.
11. SANDWEISS, D. J.: *Gastroenterology*, **1**: 965, 1943.
12. EMERY, E. S. AND MONROE, R. T.: *Arch. Int. Med.*, **55**: 271, 1935.
13. IVY, A. C., GROSSMAN, M. I. AND BACHRACH, W. H.: Peptic Ulcer, The Blakiston Company, Philadelphia, p. 917, 1950.
14. ALVAREZ, W. C.: *J. A. M. A.*, **125**: 903, 1944.
15. SCHNEDORF, J. G. AND IVY, A. C.: *J. A. M. A.*, **112**: 898, 1939.
16. RICKETTS, W. E., PALMER, W. L., KIRSNER, J. B. AND HAMANN, A.: *Gastroenterology*, **11**: 789, 1948.
17. ZAMCHEK, N., CHALMERS, T. C., WHITE, F. AND DAVIDSON, C. S.: *Gastroenterology*, **14**: 343, 1950.
18. FINSTERER, H.: *Lancet*, **2**: 303, 1936.
19. WELCH, C. E. AND ALLEN, A. W.: *New England J. Med.*, **240**: 277, 1949.
20. SMITH, F. AND JORDON, S. M.: *Gastroentrology*, **11**: 575, 1948.
21. SINGLETON, A. C.: *Radiology*, **26**: 198, 1936.

RÉSUMÉ

Le traitement de la crise aiguë d'ulcère gastro-duodénal consiste dans le repos au lit et la prise à toutes les heures d'un mélange de lait et de crême. Plus tard trois repas légers sont surajoutés à cette alimentation de base de toutes les heures. A son retour au travail, le malade pourra se permettre un régime plus libéral et alterner un antiacide minéral avec l'alimentation lactée.

Les moyens à prendre pour prévenir les attaques récurrentes sont ensuite discutés. Pour ce qui est du traitement immédiat de l'hémorragie de l'ulcère peptique, on convient que la mesure thérapeutique qui s'impose de toute nécessité est la transfusion de sang entier en des quantités convenant à chaque cas. Chez le malade âgé dont la vie est mise en danger du fait d'une hémorragie abondante et massive, la chirurgie d'urgence reste le seul moyen.

Quant à la conduite future dans le cas d'un ulcère gastrique, on devra s'inspirer de ce fait reconnu que de leur apparence de bénignité on ne peut jamais inférer l'impossibilité d'une transformation cancéreuse. En général on devrait même considérer toute lésion de ce genre comme maligne à moins de preuves contraires. La preuve consiste dans la guérison complète et le maintien de cette guérison, tel que démontré par la disparition de l'ulcère aux Rayons X, l'absence de symptômes cliniques ainsi que de sang occulte dans les selles.

ANGIOCARDIOGRAPHIC FINDINGS IN PULMONARY TUBERCULOSIS.—The authors studied 91 tuberculous patients by angiocardiography. Local areas of the lung showed diminished vascularity, depending upon the extent and severity of the involvement. Fibrosis caused displacement and distortion of the vessels in most cases. By means of angiocardiography and contrast visualization aortic aneurysm may be differentiated from hilar and mediastinal masses and lymphadenopathy. The pulmonary artery was most frequently affected by periarterial lesions.—Steinberg, I., McCoy, H. I. and Dotter, C. T.: *Dis. of Chest*, **19**: 510, 1951.

SIMPLER METHODS FOR THE AVERAGE LABORATORY

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WITH the ever increasing number of determinations required from clinical laboratories, it is felt that there is a great need for discrimination among the multitude of new methods and their suggested modifications.

The laboratory staff of small hospitals usually have neither the time nor the facilities to evaluate the precision, adaptability and simplicity of these various methods. From the clinical standpoint and having in mind the average organization of small hospital laboratories, the author feels that precision is no more important than *adaptability* and *simplicity* in the methods involved.

To this viewpoint might be opposed the fact that, from time to time, evaluations of the relative effectiveness of various methods are published which should direct the choice in routine work. Unfortunately, most of this discriminating work is accomplished by fully equipped laboratories for whom adaptability according to space, time, apparatus and personnel is not a problem, with the result that the most strongly advocated procedure is often the least adaptable.

It should be borne in mind that the average small town laboratory is not usually equipped with the latest continuous extractors, flame spectrophotometers or even automatic shaking apparatus.

Another crucial problem involved in the economical administration of a small scale laboratory is that the demand for the majority of the determinations is only intermittent. This means the constant renewal of reagents whose preparation is laborious and their stability variable. Thromboplastin stock solutions that last twenty-four hours at the utmost, cephalin-cholesterol emulsions which are to be discarded after a few days are quite a burden for small laboratories. In such cases, alternative reagents, such as stable viper venom for the former and cadmium sulphate solution for the latter are most welcome.

Hence, in addition to *simplified* procedures, there is a need for *adaptable* ones. Preference should surely go to the one which requires only the average material and, if possible, stable reagents, as long as the difference in accuracy is not clinically significant.

In photometric procedures, it would also be highly advisable to indicate the wave length required instead of an arbitrarily numbered filter, adaptable to only one brand of photocolorimeter. Spectrophotometers are scarce in the average laboratories, but one can always be informed by the manufacturer of the various wave lengths of the filters attached to his own apparatus.

With these problems in mind and a few years of personal experience in small laboratories, I suggest a few simple, readily adaptable, time-saving procedures for determinations encountered in routine practice. These methods, some of which may still be open to criticism, have nevertheless proved their effectiveness in clinical practice. Most of them have been successfully compared by us with more elaborate methods, have stood frequent repetition and have shown a recovery percentage that can be depended on. The scarcity of the steps involved reduces to a minimum the danger of errors, without significantly altering the precision.

BLOOD GLUCOSE

The simplest and yet reliable procedure we have found for blood glucose determinations is that of Benedict[1] based on the formation of a red alkaline picrate in the presence of picric acid and sodium carbonate. The colour developed may be estimated visually against standard glucose solutions or, as modified by us, photometrically at 490 mμ.

Procedure.—In a centrifuge tube, measure 0.2 ml. of whole blood, dilute with water to 1.0 ml. (This step may be used to wash blood off pipette.) Add 1.5 ml. of a saturated solution of picric acid. Mix thoroughly and centrifuge. In a pyrex test tube (preferably with a beak), evaporate almost to dryness (at point of crystallization) 1.0 ml. of the clear supernatant liquid. Add 0.5 ml. of a 20% sodium carbonate solution and again heat until crystals appear (a glass bead may be useful against bumping). Wash with small portions of water in a graduated tube and dilute to 5.0 ml. Read photometrically at 490 mμ. (Use same filter as for creatinine determination with alkaline picrate reagent.)

Calibration.—A curve can be conveniently calibrated with aliquot volumes of a 0.1% glucose solution. Use 0.2, 0.4, 0.8, 1.6, 2.4 and 3.2 ml. of standard solution. Add 0.8 ml. of saturated picric acid solution and evaporate directly in the pyrex test tube. Proceed exactly as above. These quantities correspond respectively to a glucose concentration of 25, 50, 100, 200, 300 and 400 mgm. per 100 ml. of whole blood. With suitable concentrations according to the apparatus used, a straight line is obtained on semi-logarithmic paper, as illustrated in Fig. 1.

This method which requires easily prepared and stable reagents, is sufficiently accurate to indicate abnormal glucose levels in routine practice. It can also be advantageously used in glucose tolerance tests where the general picture of the curve is much more important than the actual glucose content of the blood. Due to the interference of creatinine (normally found only in traces in the blood), this method should be less reliable in low values. It is definitely unreliable with blood glucose levels under 50 mgm. per 100 ml. of blood. It has been our practice, in such cases, to repeat the determination with 0.4 instead of 0.2 ml. of blood. The same applies to spinal fluid where glucose levels are normally much lower than in blood.

BLOOD AMYLASE

The preceding procedure for blood glucose has been applied by us in a very simple and quite satisfactory method of evaluating blood serum amylase. As only important deviations from the normal activity are significant clinically, this simple, rapid procedure gives sufficient information. From numerous controls, we have found that the normal limits were slightly higher than those of the previous methods, that is, between 80 and 200 units, a blood amylase unit being defined as the number of mgm. of glucose liberated from a starch solution by 100 ml. of serum at 40° C. during one-half hour. With this method we have found values ranging from 300 to 1,600 units in acute pancreatitis.

Procedure.—In two test tubes marked A (for amylase) and B (for blank) containing 5 ml. of a 5% starch solution, add respectively 2 and 3 ml. of physiological saline solution (0.9% NaCl). Warm to 40° C. in a water bath. Then add in tube A, 1.0 ml. of clear, non-hæmolyzed serum, mix and incubate both tubes at 40° C. for 30 minutes. Cool. To 1.0 ml. of A and B respectively, add 1.5 ml. of a saturated solution of picric acid, centrifuge and proceed exactly as for blood glucose. Read directly from blood glucose curve. Determine glucose concentration of serum using 0.2 ml. as described for blood glucose. This gives the correction for glucose already in serum (G).

Calculations.—(A – B) x 1.6 – G : Units of amylase.

When thoroughly washed starch is used, no blank is usually necessary and the preceding formula becomes: 1.6 A – G : Units of amylase.

BLOOD UREA NITROGEN

Most of the volumetric methods used in the determination of blood urea nitrogen, such as the hypobromite method, require special skill and are subject to errors which may not be readily checked by an inexperienced technician. Too many factors are involved, such as variations in temperature, in atmospheric pressure, loss of gases or intake of air. Furthermore this type of procedure which cannot be performed in series, is time-consuming, while the manipulation of bromine is always a hazard.

Probably the most widespread method now-

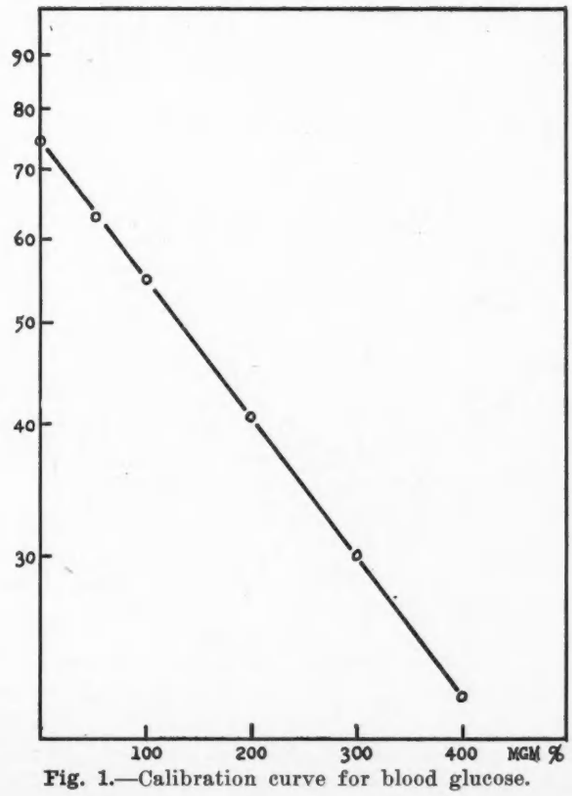

Fig. 1.—Calibration curve for blood glucose.

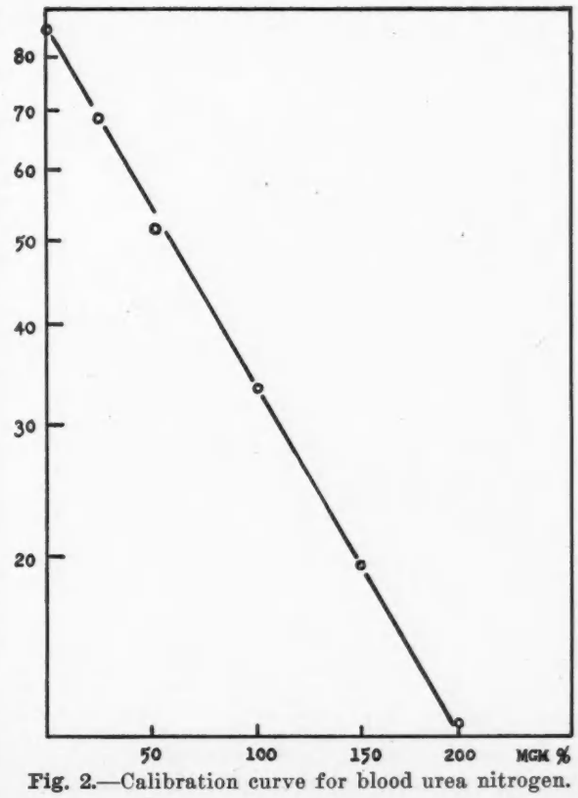

Fig. 2.—Calibration curve for blood urea nitrogen.

adays is the urease method and its numerous modifications. In spite of the popularity of this method, which in many ways is definitely superior to the volumetric ones, we have always used it with great caution. Urease, like all other enzymes, is too easily inhibited, for example, by traces of cations of heavy metals, and requires a constant control (time and temperature of incubation, etc.). In our opinion a *chemical* hydrolysis which involves less rigid control is to be definitely preferred to this type of hydrolysis of urea in ammonia. This is the reason why we have finally adopted the recent method of Kibrick and Skupp[2] which combines simplicity and adaptability with accuracy and reduces to a minimum the sources of errors. The method described below is essentially that of the authors, with slight modifications.

The principle of the method is as follows: A blood filtrate is heated under pressure with phosphoric acid. After cooling, the excess acid is neutralized by addition of an alkali. The ammonium salt resulting from the hydrolysis of urea is determined by nesslerization. This method allows determination in series and requires no complicated material. If an autoclave is not available, we have found it quite as convenient to use an ordinary household pressure cooker calibrated at 15 or 20 pounds, as suggested by the authors.

Procedure.—In a 10 or 15 ml. graduated centrifuge tube, add successively 1 ml. of serum, 8 ml. of a N/24 H_2SO_4 solution and 1 ml. of a 5% sodium tungstate solution. Shake well and centrifuge. In another graduated tube, add 1.0 ml. of clear supernatant liquid and 0.5 ml. of a 1*M* H_3PO_4 solution. Cover with aluminium foil and heat under 20 pound pressure for one hour (or under 15 pound pressure for 1½ hour). Cool and add 1 ml. of a 1*N* NaOH solution. Dilute to the 7 ml. mark with distilled water. Add 3 ml. of Nessler reagent. Mix by inversion and read photometrically at 445 mμ. (If coloration is too deep, a good approximation is obtained by diluting with distilled water and correcting for dilution.) Reject all cloudy samples. Turbidity is likely to occur if Nessler reagent is too alkaline. To check alkalinity, titrate 20 ml. of normal HCl solution with Nessler reagent. A good end point should be obtained with phenolphthalein as indicator between 11.0 and 11.5 ml.[3]

Calibration.—A curve is easily calibrated by substituting for serum different dilutions of a standard solution of urea to which has been added a little phenol as preservative. With suitable concentrations, a straight line can be plotted. Fig. 2 shows the accuracy of this simple method.

BLOOD SERUM TOTAL LIPIDS

The level of serum total lipids can be easily determined by successive extraction with a 3:1 alcohol-ether mixture and a low boiling petroleum ether (b.p. 30 to 60° C.). The weight of the residue, after evaporation of the petroleum ether, gives directly the quantity of total fats in the sample of serum, which can easily be converted in mgm. per 100 ml. of serum.

This simplified procedure which requires common solvents and no complicated material, is very satisfactory. Being a gravimetric procedure, its only inconvenient feature is that its accuracy is proportional to the volume of serum sample available. It has been our policy to perform this analysis on the pooled sera obtained for other determinations.

Procedure.—In a cylinder containing at least 10 ml. of a 3:1 mixture of 95% ethanol and ether per ml. of serum, add slowly and with constant stirring a known volume of blood serum. Let stand for at least 30 minutes with occasional stirring. Filter and wash residue twice with the alcohol-ether mixture. Evaporate combined filtrates in an evaporating dish on a water bath (under a hood or, if not available, in an efficient air draught, *away from fire*). Extract hot residue twice with petroleum ether (benzine). Evaporate combined filtrates on water bath. Allow to cool. Dry bottom of dish and weigh. Dissolve residue with petroleum ether and discard. Dry dish and weigh. The difference in weight of the dish gives the weight of total fats in the sample of serum. Express in mgm. per 100 ml. of serum. Normal is between 800 and 1,200 mgm. per 100 ml. of serum.

URINE ALBUMIN (QUALITATIVE)

The detection of albumin in routine urine analysis, apparently a simple procedure, may lead to false interpretations. It has been our experience that heat coagulation failed to reveal at times important traces of albumin. On the other hand, while sulphosalicylic acid has proved to be the most appropriate reagent for albumin detection, errors are common when urine contains an excess of phosphates or urates. To avoid these difficulties, Bernhard and Scher's[4] reagent (a mixture of equal parts of methanol and of a 20% sulphosalicylic acid solution) is of great value.

Procedure.—Transfer about 5 ml. of urine in a test tube and overlay with about 5 drops of reagent. Note the appearance of a cloudy ring. Phosphates are readily dissolved in methyl alcohol, while the interference of urates is easily eliminated by gently heating the contact zone of urine and reagent.

SUMMARY

In answer to the need for simpler and more adaptable methods for the average laboratory, a few procedures requiring no complicated material are described with slight modifications. All of them have been found to be quite reliable clinically.

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REFERENCES

1. BENEDICT, S. R. AND LEWIS, R. C.: *J. Biol. Chem.*, **20**: 61, 1915.
2. KIBRICK, A. C. AND SKUPP, S.: *Proc. Soc. Exper. Biol. & Med.*, **73**: 432, 1950.
3. GRADWOHL, R. B. H.: Clinical Laboratory Methods and Diagnosis, The C. V. Mosby Co., St. Louis, 4th ed., 1948.
4. BERNHARD, A. AND SCHER, Y.: *Am. J. Clin. Path.*, **16**: 96, 1946.

SOME PSYCHOSOMATIC ASPECTS OF INJURIES*

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IN 1944 violence and accidents were the third cause of illness in Canada accounting for 8% of the total morbidity with an annual rate of 74.6 per 1,000. Figures for the United States show that at the time of the National Health Survey (1935) some 1,740,000 people were suffering from the effects of some form or another of accidental injury. Fractures, other than head injuries, ranked third in the incidence of illness equalling the frequency of respiratory disease for the age groups 26 to 64. Civilians with orthopædic disablement over the war years were as numerous as servicemen wounded in action. When figures such as these are considered in terms of the personal and social consequences of accidents a medical problem of the greatest magnitude is revealed.

"Accidents do not happen; they are caused." Whatever the immediate circumstances of an accident might be, it occurs in a setting of human motivation. Where that motivation has morbid components it has been the object of psychiatric study[9] and can be discussed under the headings (a) of psychological factors leading to the accident and (b) psychosomatic factors influencing the course of recovery from the accident.

The psychological factors leading to the accident are those associated with general accident proneness and those explicable in terms of an individual psychopathology. The idea of a general accident proneness is raised by such a clinical observation as the increased liability of patients who have suffered a head injury to injure themselves again, particularly on the head. Flanders Dunbar[3, 4] reports that most of the accidents investigated by her were not related to dangerous environments, and that only 8% occurred in circumstances demanding skill. Nor were the accidents directly related to chance: nor did physical disease or manifest psychiatric disorder play a major rôle. However 79% of the patients had been injured before, falling was the commonest circumstance of the injury, and the accident occurred most commonly at home. Hereditary and pseudo hereditary factors (for example suggestibility) were strikingly shown in that 40 to 46% of patients gave a history of accidents in their families or near friends, a figure three times higher than that obtainable in other illnesses.

The personality of these patients prone to recurring accidents is usually that of a young person outwardly restless, vivacious, immediate in his demands and action, not able to wait, impulsive, quick in judgment, often taking a chance, boastful, not taking pleasure in intellectual pursuits but very interested in athletics and in medical and health subjects as they affect the body. They are people who rebel early against parental authority and gain independence often at the cost of buried aggression and psychological guilt. A curious feature is that the more concerned they are with their body in the sense of fearing mutilation, the more the likelihood of "accidentally" injuring themselves. While often outwardly happy-go-lucky and sociable they are inwardly aggressive: in their childhood development nail biting, enuresis and occasional delinquencies are notable.

Sherrington considered the mind as essentially serving an inhibitory function in relation to motor behaviour. He stated that the greatest relief of instinctual tension is by action, the least by phantasy, speech lying in between. On this basis it is possible to make a dynamic formulation of proneness to accident. Given a person of outgoing restless personality who emphasizes immediate action and who has little recourse to phantasy, what happens when tension mounts within himself from the pressure of guilt from conflicts and aggression? An immediate and active form of release of tension might well be a violent injury or a fracture: it might well be a matter of psychosomatic economy and a defense against his own driving activities to procure *repeatedly* a sudden break, with the reinforced rest that follows.

An individual psychopathology is sometimes revealing in cases not of necessity accident prone. It is a common experience to wake up in the morning, unrefreshed, perhaps after an unpleasant dream recalling deep conflicts, with the feeling that it is going to be a black day. The premonition is often sustained. The coffee is spilt, the feet trip, a car smash is avoided by mere luck, the new suit is stained, etc. On such

* Read at the Annual Meeting of the Ontario Medical Association, 1950.

a day a little free association will reveal some startling discoveries about oneself. As to the injured, the personal events leading to the accident, the mood of the patient preceding the accident and his own association of ideas are relevant enquiries. For example a butcher, who for years had exposed himself to the dangers of his own knife without mishap, chopped off his finger on one black morning after a quarrel with his wife about his mother-in-law.

In connection with psychosomatic factors influencing the course of recovery from accident, a distinction must be made between head injuries and injuries elsewhere. Head injuries raise all the pathophysiological problems of cerebral trauma which continue to engage the interest of the neurologist and surgeon. Even so there is no clear relationship between the apparent severity of the head injury and the clinical recovery. The majority of patients who have suffered a head injury continue to retain symptoms (60%), and a large proportion (5 to 11%) are incapacitated to some degree with symptoms ranging from headache and dizziness on the one hand to severe neurological or psychiatric disturbances on the other.

Depending on the extent and severity of the injury, on the personality of the patient, and on his subsequent handling, neuropsychiatric complications may arise at any time and persist in varying severity as follows.

1. Minor contusion (Symonds) or post-concussive syndrome.
2. Traumatic neurosis with anxiety or neurasthenia or hypochondriasis.
3. Post-traumatic disturbances of consciousness; amnesia, fugues, automatisms.
4. Hysterical reactions with conversions.
5. Unrelated psychoneurosis.
6. Post-traumatic personality changes in children and adults.
7. Korsakow's psychosis.
8. Catatonic or delirious states.
9. Post-traumatic psychosis with personality or mood changes.
10. Post-traumatic dementia (Symonds) psychasthenia or submentation (Mapother).

The minor contusion syndrome is of great importance as the basis of progressive neurotic reactions which may become chronic. Trotter[17, 18, 19] recognized the organic nature of the syndrome and that view is generally held. There may be loss of consciousness or not. After two or more days the patient complains of a dull throbbing paroxysmal headache increased by stooping, exercise, noise or excitement. Dizziness is experienced. The patient feels insecure, lacks confidence, loses sleep, and has a fear of falling. Night terrors, fatigue and irritability supervene. He may later have an increased susceptibility and intolerance to alcohol.

The meaning of the head, as the injured organ, becomes important from a psychopathological viewpoint. Man knows that *his* power over *his* universe rests in the head. When the head is attacked his potency is threatened and he becomes fearful and insecure. Special symptoms such as dizziness strengthen the insecurity. There may be a retreat to a more protected or childlike state but in dreams the threatening experience repeats itself. At a later date anxiety arising from the threat may become fixed on the body or a part of the body in the form of hypochondriasis, neurasthenia or other hysterical conversions. The condition then merges with that of traumatic neurosis.

In traumatic neurosis however the psychogenic element dominates from the start. With a manifest injury there is an acceptable excuse for a failure in living. Society is not antagonistic and the patient is almost encouraged to take up his symptoms. According to his personal psychopathology he will present anxiety or show even terror or panic. His personal fears may become converted into hypochondriacal preoccupation or they may accentuate his previous personality weaknesses.

Fenichel[8] states that "the basic function of the mental apparatus is the re-establishment of stability after a disturbance of external stimuli". This equilibrium depends largely on two factors: (a) constitutional; (b) previous experience of the environment. With regard to the former every injured person has his breaking point: in respect to the latter every patient will seek to regain control of the outer world and himself by a constant passive repetition of the experience. His preconceived ideas, his attitudes and other personality characteristics will come into play as well as the deeper emotional and symbolic meaning of the injury and its effects. For these reasons it is important to understand the patient's personality and his feelings about the injury before they become too deeply buried in his mind and changed by active defensive processes. Bringing him back mentally to the scene of the accident, letting

him reassociate on the experience and encouraging the release of emotions is both a method of investigation and of treatment (abreaction).

If the neurotic reaction is allowed to become established secondary gains may play a dominant rôle preventing recovery. While trauma mobilizes unpleasant mental conflicts, financial compensation brings not only rational advantages but also the emotional props of passive acceptance and protecting security. If compensation arrangements are prolonged in dispute and if the attitude of authority is stern and even intolerant the whole charge of mental energy may become displaced into strong feelings of resentment, even to a paranoid degree.

Post-traumatic personality changes vary from an incorporation into the personality of a new symptom like irritability to an accentuation of trends previously on the borderline of normality. Social withdrawal, lack of friendly relationship, selfishness, or paranoid trends may show themselves. Children, whose personality is as yet not fully developed, may suffer changes reminiscent of encephalitis. Behaviour disorders occur ranging from temper tantrums and facile disposition to asocial reactions like truancy, stealing, or arson.

Nothing can be said here about the more florid psychiatric categories of organic illness. They will come within the province of the psychiatrist who has the necessary facilities for care and management. But success with the neurotic manifestations starts with an appraisal, not only of the physical extent of injury, but also of the personality. Such an appraisal will be associated with an early rehabilitation program organized to include a continuing psychological awareness of the patient as a person.

Rest in bed is necessary for a few days after recovery of consciousness provided there are no major physical complications. Physical exercises should be started early and graded according to the fatigue induced. Some form of occupational therapy and a guiding time table are essential adjuvants to discipline the patient and order his mind, even if he is still confused. The childlike attitude and dependency of the patient emphasize the therapeutic aid of routine. Psychological investigations of intellectual functioning to determine deterioration or emotional changes should be carried out early in the recovery period. A return to the activities of life should be gradual and definite with the constant aim of return to full duties. Throughout, careful but guided explanations of the effect of the injury, suited to the patient's personality, are essential.

A return to full work is recommended by judging on the individual case, through a guiding scale based on the period of post-traumatic amnesia (see Table I). In making the recommendation, the kind of previous occupation should be thought of and recommendation made in the light of sequels of the head injury. For instance, allowing a highly skilled professional man to return to work with which he can no longer cope emotionally or intellectually may precipitate severe depression or suicidal thoughts. A change in occupation may be advised on psychological assessment of the patient. Finally, the social problem, and in particular, the question of compensation should be looked to.

TABLE I.

Post-traumatic amnesia	*Return to work*
5 mins. - 1 hour	6 weeks
1 - 24 hours	6 to 8 weeks
1 - 7 days	4 months
over 7 days	4 to 8 months

It is the consensus that of the greatest value in the social recovery of a patient, whether he is mildly injured or severely damaged, is that the compensation board should consider his case as early as possible. The principle should be if the Board agrees that full function has not been restored, the patient should be compensated while he is still co-operating in his rehabilitation program and not after prolonged unemployment and litigation.

The question is how early is assessment certain and fair? One may suggest that if a routine is adopted of primary assessment and regular reassessment with the major periods being 6 weeks, 3 months, 6 months and a year after the injury, but depending on the individual case, the answer to such an impossible question would be avoided.

While it is true that an injury which is likely to be permanently incapacitating is best compensated by a system of pension, it is equally true that the most psychologically useful procedure is that of an early lump sum. Here again judgment would rest on the individual case.

One of minor injury likely to have psychological sequels should be settled with an early lump sum, and one with a more severe injury should tend to be compensated early too in this way with a maximum amount at first but with a sliding scale in which the trend would be at each reassessment a diminution of the pension.

While the compensation process is carried out, with the advice of those who can appreciate psychological implication, it is paramount that the patient's doctor should encourage him to think that financial compensation means financial and personal loss in the long run, and that rehabilitation means a real compensation. In this connection it would be an economical measure to have an organization dealing with the rehabilitation and retraining of head and other injuries, with suitable training in a new vocation where necessary, and a placement officer to allow for early re-employment would be added measures.

Last, but not least, there is the question of treatment of residual disabilities. If these are psychiatric, the active co-operation of the specialist should be sought here. It can not be emphasized too strongly that if this is done only after everything else has failed and after the patient is not only disabled chronically but actually encouraged to persist in his disability by poor handling in compensation, the problem would be almost insoluble and unnecessarily so.

Other injuries than head injuries raise the same general considerations although the functional effects of damage, and the meaning of that damage in symbolic terms, are very different. This should not lead one to think, however, that there is no mental sequel. Any bodily trauma has a psychic component and those of us who have experienced it will know that it actually is the main part of the experience.

A breach of the body is also a breach of the mental boundaries and an injury to some parts of the body (like a finger of the left hand) may have a mysterious if hidden significance. The type of injury, the circumstances in which it occurred, the mental attitude of the patient and his ideas of such an injury, his proneness or otherwise to it and his mood and ideas associated preceding the injury, are relevant points of enquiry.

Also of major importance is the immediate surgical management of the injury. If this be good, psychiatric sequels are less likely in the absence of predisposition: if they be bad, they are more likely. Should the intelligent co-operation of the patient be necessary for a series of plastic or repair operations, or in physiotherapy or subsequent surgical manœuvres, it is as well to gauge his level of intelligence at the beginning.

The patient's emotional state would be gauged, for this will have a bearing, not only on his recovery from the injury, but also on his attitude to the surgeon should operative interference fail. The argument is often advanced that a busy doctor or a surgeon has not got the time for even such rough assessment. This seems an uneconomic idea, in view of the facts, for the time subsequently spent in repairing the damage (so much of it may have been psychological) will exceed by far the few minutes necessary to establish a certain warmth of feeling with the patient (rapport) during which he could ventilate his personal feelings as well as give an intelligent account of the circumstances of the accident. Such time is also well spent on account of the patient, for this initial handling is likely to determine in part his outward attitude to the injury. Failing this, when he comes to present himself eventually to a compensation board or a psychiatrist, a comparatively simple problem may have grown and become a complex psychiatric affair. Early rehabilitation and return to work are important and the question of compensation will arise here also. The principles are the same and an air of optimism and efficiency, a firm but kind attitude with regard to work and compensation, will be the main features.

Perhaps one may end one's trends of thought on this subject by an apparent paradox which arises at some stage of a progressive psychosomatic disorder, and to which Jelliffe[11, 12, 13] has drawn attention. At one point of chronicity the patient with a weak personality has come to build so much in and around his injury and physical disability, that a great deal of his mental balance is insecurely poised on this neurotic structure. At such a time enthusiastic and ill advised surgery, particularly if it is successful, is only too likely to leave the patient without his vital psychological prop and this will then precipitate him into a frank mental disease.

The paradox of a poor human result to successful organ treatment reinforces the idea that

a broad overall approach is necessary. In such an approach to injuries it is urged that the physical and psychological viewpoints be aligned continuously to the benefit of both patients and society.

REFERENCES

1. BRAIN, R. AND STRAUSS: Recent Advances in Neurology and Psychiatry, 1945.
2. BROCK, S.: Injuries of the Skull, Brain and Spinal Cord, Williams, Baltimore, 1940.
3. DUNBAR, F. AND WOLFE: *Am. J. Psychiat.*, **93**: 469, 1936.
4. DUNBAR, F.: *Am. J. Psychiat.*, **95**: 1319, 1939.
5. ELLIOT, F. A.: *Lancet*, **1**: 47, 1944.
6. ELLMEN, SAVAGE, WITTKOWER AND RODGER: *Ann. Rheumat. Dis.*, **3**: 1, 1942.
7. FETTERMAN, J. L.: *Psychosom. Med.*, **2**: 265, 1940.
8. FENICHEL, O.: Psychoanalytic Theory of Neurosis, Norton, New York, 1945.
9. FREUD, S.: Psychopathology of Every Day Life, Macmillan, New York.
10. GIRDLESTONE: *Lancet*, **11**: 765, 1945.
11. JELLIFFE, S. E.: *Internat. Clin.*, **3**: 184, 1931.
12. *Idem*: *Tr. Am. Neurol. A.*, **419**: 435, 1923.
13. *Idem*: *J. A. M. A.*, **94**: 1393, 1930.
14. KRUT, M. A.: *Am. J. Psychiat.*, **11**: 29, 1931.
15. National Health Surveys—Sickness and Medical Care Series, Bull. 4, Washington, 1938.
16. MENNINGER, K. A.: *Internat. J. Psychoanalysis*, **17**: 6, 1936.
17. REES, J. R.: The Shaping of Psychiatry by War, Norton, New York, 1945.
18. TROTTER, W.: *Lancet*, 953, November 7, 1925.
19. *Idem*: 169, January 25, 1930.
20. *Idem*: Choyce's System of Surgery, p. 388, London, 1932.
21. WECHSLER: *J. A. M. A.*, **104**: 519, 1935.

BLOOD ALCOHOL LEVELS IN RELATION TO DRIVING*

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THE blood alcohol concentrations which increase the likelihood of drivers to have accidents, for the most part have been estimated indirectly by experimental methods. Laboratory experiments such as those of Goldberg,[1] Newman and Fletcher,[2] and Carlson and his associates[3] as well as numerous psychological studies,[4] have led to the wide acceptance of 0.05 parts per hundred as the minimum concentration at which some drivers are significantly affected. In a recent experiment, Bjerver and Goldberg[5] demonstrated with practical road tests that the performance of some drivers is impaired at concentrations as low as 0.03 parts per hundred.

One of the few attempts to determine the rôle of alcohol in actual driving situations was undertaken by Holcomb[6] in Illinois. His data indicate that the incidence of accidents in a group of drivers having blood alcohol concentrations in the range of a trace to 0.06 parts per hundred was significantly increased. Unfortunately, the sample of drivers selected from the general population and the sample of drivers involved in accidents were not comparable. The present report comprises an analysis of the alcohol data obtained in a recent survey of traffic accidents.* The results pertain to the concentrations of alcohol which are important in *actual* driving situations.

The 919 drivers included in this survey represent 93% of those involved in personal-injury motor vehicle accidents in the City of Toronto between May 17 and August 17, 1950. The "intoximeter"[7] was employed for the indirect determination of blood alcohol concentrations through breath analysis. Prior to the survey, our laboratory results with this method had indicated agreement within 15% of the blood alcohol concentrations determined by direct analysis of blood (using our modified desiccation[8] method). During the survey, breath samples were obtained by police officers from 59% (542) of the drivers in the series. This group included 77% of those whom they considered "had been drinking". It was estimated from all the available data that 23% of the drivers (involved in 30% of the accidents) in the survey had more than a trace of alcohol in their blood; breath samples were actually obtained from 138 (75%) of these.

Most of the information upon which the following analysis is based was obtained from the official accident reports. These were prepared by police officers specially trained in accident investigation. Since their reports were often presented in court, they were as objective, accurate, and complete as possible in their description of the accident. Each report included a record of

* This work was supported by a Dominion Public Health Grant and was presented at the First International Conference on Alcohol and Traffic in Stockholm, September, 1950.

* This survey was designed to estimate the relative importance of various factors in accidents including age, alcohol, accident-proneness, and exposure. The analysis of the relationship between these various factors is not yet complete.

the mechanical condition of the vehicles, the presence or absence of obstructions to vision or other environmental hazards, the physical condition of the drivers, as well as a summary description of the total accident situation. In addition, the various driving errors leading to the accident were classified and recorded. The proportion of drivers who made errors, definite enough to be noted by the investigating officers, have been related to their blood alcohol concentrations in Table I.

TABLE I.

THE RELATIONSHIP BETWEEN BLOOD ALCOHOL CONCENTRATIONS AND THE INCIDENCE OF DRIVING ERRORS

Blood alcohol concn. of drivers (parts per 100: breath method)	*Total No. of drivers*	*No. of drivers making errors*	*Percent of drivers making errors*
0.00	238	94	39.5
0.01 to 0.04	28	9	32
0.05 to 0.14	48	25	52
0.15 or over	21	18	86

The percentage of drivers making errors markedly increases with increase in blood alcohol concentration. Since impaired judgment in driving is probably manifested by errors, it would appear that the effect of alcohol on judgment can be illustrated in a practical way with reference to increased frequency of driving errors.

However, it was felt that the rôle of alcohol in traffic accidents could be indicated more clearly if the contribution of each driver to his own accident were expressed as a score. In the estimation of a score, due allowance was made for contributing factors which were clearly beyond a driver's control, such as mechanical defects or environmental hazards. Thus, for each accident, ten points were apportioned between those factors which could be directly attributed to the drivers concerned, and those factors beyond their control. The points assigned to the drivers involved in a particular accident, were divided between them as a score, on the basis of what appeared to be their relative contribution to their accident, as judged from all available data.

The "relative contribution scores" for all drivers in the series were determined independently by each of us (without knowledge of the blood alcohol concentrations) and the results compared. It was found that the same scores had been assigned in two-thirds of the cases, while in the remainder the agreement was within three points on the arbitrary scale of ten. In the latter cases, agreement was reached after further investigation. Since it may be objected that only a rough assignment of scores is possible, only the very high (8 to 10) and the very low (0 to 2) "relative contribution scores" have been used in the analysis which follows.

In Table II the frequencies of drivers with high and low scores are shown with corresponding blood alcohol concentrations.

The proportion of drivers in the group having appreciable alcohol values (0.01 or over) who were assigned high scores was found to be significantly greater than in the group with no alcohol (χ_2=30.5). Furthermore, it was determined that this difference first became significant in the 0.03 to 0.05% range of concentrations (χ_2=4.9). Examination of the accident reports revealed that only one out of eight drivers with a concentration in this range was reported by the investigating officer as having "been drinking". Thus there is little possibility of bias either in the accident reports or in our assessment of contribution scores due to a knowledge of the presence of alcohol in this range of concentrations.

TABLE II.

THE RELATIONSHIP BETWEEN BLOOD ALCOHOL CONCENTRATIONS AND RELATIVE CONTRIBUTION SCORES

Scores of drivers	*Blood alcohol concentrations*							
	0.00	0.01 to 0.02	0.03 to 0.05	0.06 to 0.08	0.09 to 0.11	0.12 to 0.14	0.15 to 0.17	0.18 or over
	(Numbers of drivers having these concentrations)							
8-10 (A)	86	1	19	9	14	6	13	8
0-2 (B)	176	10	18	4	3	3	1	0
Ratio $\frac{(A)}{(B)}$	0.5	0.1	1.1	2.3	4.7	2.0	13.0	—

At the opposite extreme of the range, it should be noted that 21 out of 22 drivers who had blood alcohol concentrations of 0.15 parts per hundred or higher were considered to be almost entirely responsible for their accidents ("relative contribution scores" in the range 8 to 10). In this group (blood alcohol concentrations of 0.15 parts per hundred or higher), there were 43 times as many drivers with high "relative contribution scores" (8 to 10) as would be expected on the basis of the distribution of scores in the group with no alcohol in their blood. The isolated driver with a blood alcohol concentration of 0.15 parts per hundred and a score of 0 had been stopped at an intersection for some minutes by a red traffic signal. His car was struck in the rear by that of another driver (blood alcohol: 0.10%; relative contribution: 10). Therefore, he could not be considered to have contributed to this accident. Under these circumstances his participation in this accident was purely passive.

There are several extreme cases within the data which suggest something of the range of individual variability in the effect of alcohol upon drivers. For example, one driver who had a blood alcohol concentration of 0.03% and a "relative contribution score" 10, was involved in an accident while "weaving" his car down a busy street. Another driver—blood alcohol 0.14%, "relative contribution score" 0—avoided a careless pedestrian with a show of considerable skill and control. He became involved in an accident only when a second driver (blood alcohol 0.00%) ran into both him and the pedestrian.

DISCUSSION

These data indicate that the minimum concentrations of alcohol which are important in actual driving situations, are in the range of 0.03 to 0.05 parts per hundred. These concentrations are similar to those which have been shown to affect driving performance.[5] Moreover, the results of physiological[1, 2] and psychological studies[4] have indicated indirectly that these concentrations are the ones which are likely to affect drivers. Therefore, the present survey of accidents, which points up the rôle of alcohol in actual driving situations, tends to confirm the results obtained from practical road tests and in laboratory experiments.

The one driver in this study who had a blood alcohol concentration of 0.15 parts per hundred and a contribution score of 0, played an entirely passive rôle in his accident. This case illustrates the limitations of this method of assessing the rôle of alcohol in accidents. The data do not yield relevant information regarding the concentration of alcohol which affects all drivers. However, the results are consistent with the presumption that all drivers are affected at concentrations of 0.15 parts per hundred. Holcomb[6] found 55 times as many drivers in an accident group having blood alcohol values of 0.15 parts per hundred or higher, as would be expected on the basis of the number of accident-free drivers found with this concentration. In this survey there were 43 times as many drivers with this concentration or higher who had high "relative contribution scores" as would be expected on the basis of the proportion of those with high scores and no alcohol in their blood.

From the available evidence, it appears quite reasonable to *presume* that most drivers are not significantly affected by concentrations of alcohol less than 0.05 parts per hundred and that all drivers with concentrations of 0.15 parts per hundred or higher are affected. These two concentrations adequately describe the range of variation in the effects of alcohol for all but a few exceptional drivers. On biological grounds the existence of such exceptional drivers must be admitted but it is reasonable also in application of rules and penalties that they prove themselves to be exceptions. The range of variation for ordinary drivers is between 0.05 and 0.15 parts per hundred. However, only some drivers within this range of concentrations are noticeably impaired. It has been stated[9] that "the chief problem is not the driver who was so intoxicated that he was physically unable to drive a car. . . . The difficulty is with sub-clinical intoxication—that degree which has enabled the driver involved in the accident to appear normal at the material time but which at the same time had definitely impaired his driving efficiency". It would appear that the available clinical tests are not sensitive enough to reveal this condition. Furthermore, such tests do not afford a relevant measure of the complex adjustments essential to safe driving. On the other hand, it would appear that evidence of improper driving behaviour could provide a sensitive and relevant test of the presence of "subclinical intoxication". It is suggested that evidence of blood alcohol concentrations of 0.05 parts per hundred or higher, together with evidence of driving errors,

may be sufficient to designate those drivers who may be presumed to be affected by alcohol.

CONCLUSIONS

1. This study indicates that the minimum concentration of alcohol in the blood at which drivers are significantly affected is in the range of 0.03 to 0.05 parts per hundred. In this respect, these data which pertain to actual driving situations, support the results of laboratory experiments, practical road tests and previous surveys.

2. The results of this survey are consistent with the presumption, largely based on experimental evidence, that all drivers are affected when their blood alcohol concentrations are 0.15 parts per hundred or higher.

For making this study possible, our thanks are due to the Attorney General's Department of the Province of Ontario, and to the Toronto City Police, in particular to Chief Constable Chisholm, Inspector Page, and the Accident Investigation Bureau. Our thanks are also due to Professors J. K. W. Ferguson and G. H. W. Lucas for their many constructive suggestions throughout this work and the preparation of this paper. We gratefully acknowledge the advice on statistical treatment made by Professor B. A. Griffith, and the technical assistance of Mr. J. West.

REFERENCES

1. GOLDBERG, L.: Quantitative studies on alcohol tolerance in man. The influence of ethyl alcohol on sensory, motor and psychological functions referred to blood alcohol in normal and habituated individuals, *Acta Physiol. Scand.*, **5**: (Suppl. 16), 1, 1943.
2. NEWMAN, H. W. AND FLETCHER, E.: The effect of alcohol on driving skill, *J. A. M. A.*, **115**: 1600, 1940.
3. CARLSON, A. J. *et al.*: Studies on the possible intoxication action of 3.2 per cent beer. University of Chicago Press, Illinois, pp. 85, 1934.
4. JELLINEK, E. M. AND MCFARLAND, R. A.: Psychological experiments on the effects of alcohol, *Quart. J. Stud. Alc.*, **1**: 272, 1940.
5. BJERVER, K. AND GOLDBERG, L.: Effect of alcohol ingestion on driving ability. Results of practical road tests and laboratory experiments, *Quart. J. Stud. Alc.*, **11**: 1, 1950.
6. HOLCOMB, R. L.: Alcohol in relation to traffic, *J. A. M. A.*, **111**: 1076, 1938.
7. JETTER, W. W. AND FORRESTER, G. C.: The perchlorate method for determining concentration of alcohol in expired air as a medicolegal test, *Arch. Path.*, **32**: 828, 1941.
8. SMITH, H. W.: The specificity of the desiccation method for determining alcohol in biological fluids. In press, 1951 (*J. Lab. & Clin. Med.*)
9. RABINOWITCH, I. M.: Medicolegal aspects of chemical tests of alcoholic intoxication, *Am. J. Police Science*, **39**: 225, 1948.

DIABETES MELLITUS AND PREGNANCY*

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PRIOR to the discovery of insulin the problem of the pregnant diabetic was practically non-existent. Most diabetic women were sterile, and in one series[1] of female diabetics only 2% became pregnant. However, since the introduction of insulin therapy and the better control of the diabetic state, fertility in the diabetic has reached an almost normal frequency, and one meets now with a fairly large number of pregnant diabetics. Moreover, whereas prior to the introduction of insulin therapy the pregnant diabetic frequently lost her life from the occurrence of acidosis or infection or both, proper diabetic control has reduced these two dangerous complications to a minimum and has made it very safe for the diabetic mother. Maternal mortality is now no greater among pregnant diabetics than among pregnant non-diabetics. The problem, however, that faces the internist and the obstetrician is that of the high fetal mortality. Miscarriage in late pregnancy, stillbirth and neo-natal death are frequent accidents in diabetic pregnancies. Together they account for a very high incidence of fetal death. Furthermore, the incidence has remained high since the discovery of insulin and the introduction of good diabetic control with various types of insulin and more advanced dietary measures.

Many reports have appeared in the literature in the past twenty years dealing with the association of diabetes mellitus and pregnancy. The intention has usually been to emphasize the problem as outlined above, and to attempt to find the underlying cause. In this report I am presenting a fairly large series of pregnant diabetics, indicating the main characteristics of the condition, and attempting to correlate various factors in the hope of shedding some light on the cause or causes of the high fetal mortality.

MATERIAL FOR STUDY

This report is concerned with the case histories of 84 pregnancies occurring in 73 diabetics who were admitted to the wards of the Royal Victoria Hospital and the Royal Victoria Montreal Maternity Hospital in the period from 1929 to 1949. Fifty-five per cent of these patients were under the care of the Metabolism Department of the former hospital throughout the pregnancy; 24% received their diabetic treatment elsewhere. In 21% the diabetes was discovered for the first time only during the latter weeks of pregnancy. The diabetes was usually treated with a low-fat,

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high-carbohydrate diet, the values usually being 80 to 90 gm. protein, 50 gm. fat, and about 200 gm. carbohydrate. The insulin administered was either crystalline zinc or protamine zinc or both. Attempts were made to keep the blood sugar levels as close to the normal as possible and to avoid glycosuria, except where it was felt that the renal threshold was low.

Effect on the mother.—All of the 73 mothers survived the pregnancy and the puerperium. This 100% maternal survival occurred in spite of six cases of diabetic acidosis in the terminal stages of the pregnancy. Thus the prognosis for the mother is very good. This is in agreement with practically all the reports in the literature since the discovery of insulin, and emphasizes how safe it is for the diabetic to become pregnant provided her diabetes is properly supervised.

Effect on the fetus.—The prognosis for the fetus is a very gloomy one in practically all reports. White and Hunt[2, 3] report a fetal mortality rate of 33% from 1922 to 1938 at the Geo. F. Baker Clinic where the diabetes is efficiently supervised. Lavietes, Leary, Winkler and Peters[4] report from Yale a fetal mortality of 40% in 31 pregnancies occurring in 23 diabetic mothers. Lawrence and Oakley[5] in England report a fetal loss of 37% out of a series of 54 pregnancies in 44 diabetics. Similarly poor fetal results have been reported by Palmer and Barnes[6] and many others. Our own series of 84 pregnancies resulted in 59 live fetuses (70%) and 25 dead ones (30%).

In an effort to clarify the reasons for such disappointing results we have gathered various data, and have attempted to correlate these data with the fetal results.

Relation of previous pregnancies to fetal results. — Palmer and Barnes[6] claim that the para of the pregnancy has no effect on the fetal survival. We have divided our own cases into primiparæ and multiparæ and have correlated them with the fetal results in Table I.

TABLE I.
RELATION OF PREVIOUS PREGNANCIES TO FETAL RESULTS

	Primparæ		*Multiparæ*	
	Cases	*%*	*Cases*	*%*
Living fetuses	23	79	37	67
Dead fetuses	6	21	18	33

The primiparæ show a fetal survival of 79% as compared with 67% in multiparæ. The prognosis for the primiparous diabetic is therefore a much better one than for the multiparous.

Relation of age of mother to fetal results.—Does the age of the mother affect the fetal survival? Mosenthal[7] found that the infant mortality increased distinctly when the mother was over 30 years of age. Patterson and Burnstein[8] found that diabetics over 35 years of age had a fetal mortality of 50%, while those under 35 years had a fetal mortality of only 39%. Our own data are analyzed in Table II.

TABLE II.
RELATION OF AGE OF MOTHER TO FETAL RESULTS

	Mothers under 30 years		*Mothers 30 years and over*	
	Cases	*%*	*Cases*	*%*
Living fetuses	25	68	34	72
Dead fetuses	12	32	13	28

Our figures fail to confirm the above reports. Indeed, the offspring of mothers in the older age group show a slightly higher survival rate, namely 72%, as compared with 68% in the lower age group.

Relation of duration of the diabetes to fetal results.—The effect of the duration of the diabetes upon the fetal outcome is of obvious interest in view of the commonly observed fact that degenerative changes, especially in the vascular tree, increase with the duration of the diabetes. Arteriosclerosis of the pelvic arteries has been frequently observed in diabetic females, and this finding in the mother is claimed to be a poor prognostic sign for the fetus.[9] Palmer and Barnes[6] claim that the mother who developed her diabetes during childhood showed the greatest risk to the fetus. Miller, Hurwitz and Kuder,[10] on the other hand, infer that the duration of the diabetes has little or no effect on the risk to the fetus and, indeed, claim a high fetal mortality even many years before the mother developed her diabetes.

We have divided our own cases into two groups, those in which the duration of the diabetes has been 5 years or less, and those in which the duration of the disease has been greater than 5 years. Our results are shown in Table III.

TABLE III.
RELATION OF DURATION OF DIABETES TO FETAL RESULTS

	Diabetes 5 years or less		*Diabetes longer than 5 years*	
	Cases	*%*	*Cases*	*%*
Living fetuses	39	71	15	65
Dead fetuses	16	29	8	35

Our figures indicate a fetal survival of 71% where the diabetic condition of the mother has lasted only five years or less, as compared with 65% where the diabetes has lasted longer than five years. This difference is statistically significant and points to a better prognosis where the diabetes has been only of short duration.

Relation of age of onset of diabetes to fetal results.—We thought it might be of value to investigate the influence of age of onset of the diabetes upon fetal results. We were led to this inquiry mainly through our interest in the question of what happens when the juvenile diabetic grows up and becomes pregnant. We divided our cases with respect to the age of onset of the disease into three groups, classifying the juvenile diabetics in group 1, *i.e.*, where the diabetes commenced up to and including the age of 15 years. Table IV gives our findings.

TABLE IV.

RELATION OF AGE OF ONSET OF DIABETES TO FETAL RESULTS

	1 to 15 years		*16 to 25 years*		*26 years and over*	
	Cases	*%*	*Cases*	*%*	*Cases*	*%*
Living fetuses....	7	64	20	71	29	74
Dead fetuses.....	4	36	8	29	10	26

Our data show the lowest fetal survival, namely 64%, in the juvenile group. Where the age of onset of the diabetes was 16 to 25 years the fetal survival was higher, namely 71%. It was highest, namely 74%, where the diabetes developed beyond the age of 25 years. There is thus a steady increase in fetal survival as the diabetes develops later in life.

It is of interest that 7 out of 11 pregnancies occurring in juvenile diabetics terminated in live children. These occurred in 6 juvenile diabetic patients whose case histories are detailed below for the purpose of emphasizing that even juvenile diabetics may become pregnant and deliver normal, living children.

CASE 1

F.F., diabetic since the age of seven years. Duration of diabetes at the time of pregnancy was 22 years. Taking 44 units insulin. Blood pressure 140/90; œdema present. Delivered a normal child spontaneously 6 weeks before term while Cæsarean section was being contemplated. Weight of child 2,870 gm.

CASE 2

S.T., diabetic since the age of 13 years. Duration of diabetes at the time of delivery was 17 years. Taking 88 units insulin. Delivered a normal child by Cæsarean section at 34 weeks. Weight of child 3,900 gm.

CASE 3

C.G., diabetic since the age of thirteen years. Gave birth to normal living children at ages of 22 and 27 years. On both occasions delivered by Cæsarean section at term. Taking 80 to 90 units insulin. One child weighed 3,400 gm. and the other 3,550 gm.

CASE 4

K.L., diabetic since the age of four years. Duration of diabetes at time of delivery was 18 years. Taking 72 units insulin. Delivered a normal child by Cæsarean section at term. Weight of child 4,100 gm.

CASE 5

J.B., diabetic since the age of 15 years. Duration of diabetes at time of delivery was nine years. Taking 68 units insulin. Had much œdema and had gained much weight. Delivered a normal child by Cæsarean section at 36 weeks. Weight of child 3,170 gm.

CASE 6

C.R., diabetic since the age of 11 years. Duration of diabetes at time of delivery was 12 years. Taking 45 units insulin. Delivered a normal child by Cæsarean section one month before term. Weight of child 3,140 gm.

These cases teach us that even juvenile diabetics, whose diabetes has been present up to 22 years and who require up to 90 units insulin, may still become pregnant and deliver normal, healthy children.

Relation of the severity of diabetes to fetal results.—Miller, Hurwitz and Kuder[10] contend that the severity of the diabetes has no effect upon fetal survival. These authors claim that they find the fetal mortality high even long before the mothers developed clinical diabetes. Patterson and Burnstein[8] found in their series that when the mothers required insulin the fetal mortality was 53%, as compared with 33% when the mothers did not require insulin. Our own cases are analyzed according to the severity of the diabetes in Table V.

TABLE V.

RELATION OF SEVERITY OF DIABETES TO FETAL RESULTS

	No insulin		*Less than 40 U. insulin*		*40 U. insulin and over*	
	Cases	*%*	*Cases*	*%*	*Cases*	*%*
Living fetuses....	14	74	19	76	25	66
Dead fetuses.....	5	26	6	24	13	34

Our data show no significant difference in the fetal survival rate between the group that does not require insulin and the one requiring less than 40 units. However, the group of severe diabetics who require more than 40 units insulin shows a fairly marked decrease in the fetal survival, namely 66% as compared to 74 and 76% in groups 1 and 2 respectively.

Relation of acidosis to fetal results.—Diabetic acidosis in the mother is very dangerous to the fetus. This is clearly indicated in our series of six patients who entered the hospital in acidosis. All these cases delivered stillborn. On the other hand all the mothers recovered.

Relation of toxæmia of pregnancy to fetal results.—In recent years Priscilla White[2, 3, 9, 11] has written a great deal about the frequent occurrence of toxæmia of pregnancy in diabetics and its adverse effect upon fetal survival. She states that of a large group of cases who delivered dead fetuses signs of toxæmia antedated the accident in 80%. Lavietes, Leary, Winkler and Peters,[4] on the other hand, do not believe that the high fetal loss of diabetic pregnancies is due to toxæmia. Laurence and Oakley[5] diagnosed toxæmia of pregnancy only when all the three signs of albuminuria, hypertension and œdema were present; they had five such cases, and all of these delivered live babies. In a series of 54 pregnancies in diabetics they did not find any case of severe toxæmia with eclamptic or pre-eclamptic manifestations.

In our series, 25 cases showed signs of toxæmia of pregnancy; the diagnosis was made wherever either albuminuria, hypertension over 140/90, or œdema was present. In this group of 25 cases the fetal mortality was only 32%. This compares with a fetal mortality of 30% in the entire series of 84 pregnancies. Furthermore, two of the eight mothers who delivered dead fetuses had diabetic acidosis in addition to toxæmia of pregnancy. Our data, therefore, do not substantiate the claim that in pregnant diabetics toxæmia of pregnancy in the mother antedates or is an important cause of death of the fetus.

Relation of fetal death in previous pregnancies to fetal results.—Many diabetic patients have been advised against becoming pregnant again solely because one or more previous pregnancies terminated in fetal deaths. Such advice is based upon the poor prognosis frequently given a pregnant diabetic who has previously lost a child. Our findings do not justify such a prognosis. In our series of cases 29 out of the 55 multiparæ had previously suffered one or more miscarriages, stillbirths or neonatal deaths. These 29 cases now had a fetal mortality of 10 or 34%. This is not much greater than the fetal mortality of 33% in the total number of multiparæ.

Relation of mode of delivery to fetal results.—The question whether to allow a diabetic to go on to term and deliver spontaneously or to do a Cæsarean section before term has been widely debated. Wilder[12] believes in early section. White[9] believes that the incidence of still birth has been reduced by Cæsarean section early in the eighth month. Others, as Herrick and Tillman,[13] believe that Cæsarean section should be reserved for those cases in which there are obstetrical indications. Table VI indicates the modes of delivery and the results in our cases.

TABLE VI.

RELATION OF MODE OF DELIVERY TO FETAL RESULTS

	Spontaneous delivery		*Induction of labour*		*Cæsarean section*	
	Cases	*%*	*Cases*	*%*	*Cases*	*%*
Living fetuses....	27	64	11	65	23	92
Dead fetuses.....	15	36	6	35	2	8

There were only two fetal losses in the cases submitted to Cæsarean section. One of these children died two days and the other four days after birth. These results argue strongly in favour of Cæsarean section. The operation was usually done one to six weeks before term and only in a few cases at term. On the other hand, induction of labour, as shown in the above figures, did not reduce the fetal mortality; the results are the same in the cases that delivered spontaneously as in those in whom labour was induced.

Relation of serum prolan to fetal results—For some years Priscilla White[2, 3, 9, 11] of the Geo. F. Baker Clinic in Boston has claimed that in pregnant diabetics there was an important relationship between the level of chorionic gonadotropin in the blood and the imminence of toxæmia of pregnancy and fetal death. She has claimed that an abnormal rise of chorionic gonadotropin after the 20th week of pregnancy to a level of 200 R.U. per 100 c.c. blood or over predicts in diabetics premature delivery, stillbirth and neonatal death. Recently she stated:[11]

> "Thus, when the hormonal balance was normal as it was in 68 cases the maternal survival was 100%, the fetal survival 97%, the incidence of pre-eclampsia 2% and of premature deliveries 0. Where the balance was abnormal as it was in 58 cases the material survival was 100%, the fetal survival 47%, the incidence of pre-eclampsia 50% and of premature deliveries 40%."

In 13 of our pregnant diabetic patients the chorionic gonadotropin in the blood was estimated in the Endocrinology Laboratory of the

McGill University Clinic. It was found in this laboratory that in non-diabetic, normal pregnant patients the prolan does not rise above 1,500 I.U. per 100 c.c. blood after the 24th week of pregnancy. In five of our series of 13 patients the serum prolan was normal; four of these delivered live children and one delivered a dead one. In eight patients the serum prolan was abnormally high; these eight pregnancies resulted in six live children and two dead ones. This small series of cases, therefore, does not show any relationship between serum prolan and fetal death.

FETAL WEIGHT

That the birthweight of the child of a diabetic mother is frequently much greater than the average normal has been known for many years and has been emphasized time and again in diabetic and obstetrical literature. Indeed it is so common to see the diabetic deliver a large and sometimes giant fetus that the obstetrician will frequently question whether a patient has diabetes only because she delivered an overweight child. This excess weight of diabetic offspring is due partly to œdema, partly to excess fat,[7] and partly to increase in size of the thoracic and abdominal organs as the heart, adrenals, genitals and extramedullary erythropoiesis.[14]

In our series the average living child weighed 3,606 gm., and the average dead fetus 2,778 gm. This compares with an average normal of 3,250 gm. Furthermore, these average figures were derived from all the cases, many of which were born before term and some even at 28 and 32 weeks. When we derived the average weight of the cases delivered at term, the figure was 3,850 gm.for live children and 3,854 gm. for dead ones. Those born at 36 to 39 weeks gave average figures of 3,435 gm. for live children and 3,277 gm. for dead fetuses. That is, children born of diabetic mothers even at 36 to 39 weeks weighed more than the average child of non-diabetic mothers delivered at term. Furthermore, there is no striking difference in the average weights of live and dead fetuses born at the same period of the pregnancy. There is certainly no indication that increased fetal weight predisposes to fetal death.

Seventeen of the entire series of children weighed over 4,000 gm.; and of these 8 weighed over 4,500 gm., 5 over 5,000 gm. and 2 over 5,500 gm.

The factors responsible for the excess weight are unknown. Lavietes, Leary, Winkler and Peters[4] found no correlation between toxæmia of pregnancy and high fetal weight; neither did they find any relation of the severity or control of the maternal diabetes to the large size of the fetus. Potter and Adair,[15] on the other hand, claim that fetal overweight is due to poor control of the mother's diabetes. Similarly, Lawrence and Oakley[5] found that the cases that had the best supervision of the diabetes delivered the smallest children, and those with no supervision of the diabetes delivered the largest ones. This raises the question whether hyperglycæmia in the mother might not result in the excess deposition of fat in the fetus. In our series the average weight of the children delivered at term whose mothers did not have any diabetic treatment until the end of the pregnancy was 3,949 gm., and the average weight of full-term children whose mothers suffered of toxæmia of pregnancy was 3,927 gm. These figures compare with an average weight of all full-term children of 3,850 gm. and of full-term dead fetuses of 3,854 gm. There is, therfore, a question that poor or no diabetic treatment as well as toxæmia of pregnancy may each increase fetal weight to a small degree.

We were also curious to know whether the severity of the diabetes had any effect upon fetal weight. Our cases were divided into three groups according to the severity of the diabetes. In those requiring no insulin the average fetal weight at term was 3,743 gm.; in those taking less than 40 units insulin it was 4,162 gm.; and in those taking 40 units insulin or more it was 3,695 gm. These figures do not show any correlation between the severity of the diabetes and fetal weight.

The prediabetic fetus.—In recent years it has been noticed that infants born prior to the development of diabetes in the mother tend to be overweight. Miller[16] and Miller, Kuder and Hurwitz,[10] after reviewing the histories of known diabetics, concluded that the number of overweight babies, the neonatal death rate and stillbirth rate were much increased for as long as 20 years before clinical diabetes appeared. Similarly, Kriss and Futcher[17] claim that the average birthweight of infants of prediabetic mothers is greater than those born to normal mothers. These authors state that the

birthweight of an infant over 10 lb. may herald the development of diabetes in the mother.

In reviewing our case histories we found evidence of 7 patients who gave birth to 16 infants whose birthweight was over 4,000 gm. some time before the mothers developed diabetes. The figures are found in Table VII.

TABLE VII.

PRE-DIABETIC FETAL WEIGHT

Case	*Birthweight*	*No. of years before development of maternal diabetes*
1.	4,000 gm.	2
2.	(a) 5,130 "	unknown
	(b) 4,920 "	unknown
3.	4,560 "	1½
4.	(a) 4,400 "	6
	(b) 4,800 "	5
	(c) 5,325 "	2
5.	(a) 4,200 "	15
	(b) 4,080 "	13
	(c) 4,320 "	11
	(d) 5,040 "	8
	(e) 5,760 "	4
	(f) 6,720 "	9
	(g) 5,280 "	2
6.	4,260 "	4
7.	4,320 "	14

It is interesting to note that case 5 gave birth to 7 overweight children in the period of 2 to 15 years before the development of her diabetes. Subsequent to the onset of this disease she delivered two normal children who weighed 5,250 gm. and 5,710 gm. The group of cases in Table VII definitely indicates a tendency for the prediabetic fetus to be large. These cases are probably not the only ones of the entire series of 73 patients who demonstrate this phenomenon; it is only that the case records of the other patients did not contain any information on this subject.

CONCLUSIONS AND SUMMARY

1. A series of 84 pregnancies in 73 diabetics is presented and analyzed.

2. The maternal survival was 100%.

3. The fetal mortality was 30%.

4. Multiparæ showed a much higher fetal mortality than primiparæ.

5. The age of the mother showed no effect upon the fetal mortality rate.

6. Long duration of the diabetes increased the fetal mortality.

7. Juvenile diabetics showed a very high fetal mortality rate. The older the mother at the onset of her diabetes the lower the fetal mortality.

8. Severe diabetics showed a higher fetal mortality rate than mild diabetics.

9. All our cases of diabetic acidosis terminated in death of the fetus.

10. There was no relationship between signs of toxæmia of pregnancy and fetal death rate.

11. There was no relationship between the level of the serum prolan and fetal death rate.

12. A series of multiparæ in whom one or more previous pregnancies had resulted in fetal death showed no higher fetal death rate than other multiparæ.

13. Cases submitted to Cæsarean section showed a very low fetal mortality, namely 8%.

14. The average fetus born at term weighed 3,850 gm. Seventeen weighed over 4,000 gm. There was no difference in the average weights of live and dead fetuses born at the same period of the pregnancy. Poor or no diabetic treatment resulted in a somewhat greater average fetal weight. Toxæmia of pregnancy also caused a small increase in the average fetal weight.

15. A series of 16 fetuses, weighing over 4,000 gm. and born 2 to 15 years before the development of the diabetes in the mother, is also presented.

The author wishes to express his grateful appreciation to Dr. E. H. Mason, director of the Department of Metabolism, for encouragement and advice in this work, and to Dr. N. W. Philpott, Obstetrician and Gynæcologist-in-chief, for permission to report the obstetrical data of the cases studied.

REFERENCES

1. SKIPPER, E.: *Quart. J. Med.*, **2**: 353, 1933.
2. WHITE, P. AND HUNT, H.: *J. A. M. A.*, **115**: 2039, 1940.
3. *Idem*: *J. Endocrinol.*, **3**: 500, 1943.
4. LAVIETES, P. H., LEARY, D. C., WINKLER, A. W. AND PETERS, J. P.: *Yale J. Biol. & Med.*, **16**: 151, 1943.
5. LAWRENCE, R. D. AND OAKLEY, W.: *Quart J. Med.*, **11**: 45, 1942.
6. PALMER, L. J. AND BARNES, R. H.: *West. J. Surg.*, **53**: 195, 1945.
7. MOSENTHAL, H. O.: *Bull. New York Acad. Med.*, **18**: 217, 1942.
8. PATTERSON, MC. L. AND BURNSTEIN, N.: *Arch. Int. Med.*, **83**: 390, 1949.
9. JOSLIN, E. P.: The Treatment of Diabetes Mellitus, 6th ed., Lea & Febiger, Philadelphia, 1937.
10. MILLER, H. C., HURWITZ, D. AND KUDER, K.: *J. A. M. A.*, **124**: 271, 1944.
11. WHITE, P.: *Proc. Am. Diabetes A.*, **6**: 257, 1946.
12. WILDER, R. M.: Clinical Diabetes Mellitus and Hyperinsulinism, Saunders, Philadelphia, 1940.
13. HERRICK, W. W. AND TILLMAN, A. J. B.: *Surg., Gynec. & Obst.*, **66**: 37, 1938.
14. MILLER, H. C.: *Am. J. M. Sc.*, **209**: 447, 1945.
15. POTTER, E. L. AND ADAIR, F. L.: *Am. J. Obst. & Gynec.*, **35**: 257, 1938.
16. MILLER, H. C.: *J. Pediat.*, **29**: 455, 1946.
17. KRISS, J. P. AND FUTCHER, P. H.: *J. Clin. Endocrinol.*, **8**: 380, 1948.

STUDIES ON THE PATHOGENESIS OF DIABETES*

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TWO tributes should be repeatedly paid to Frederick Grant Banting. One is to recall his great personal qualities. This has been done affectionately on many occasions by those who had the privilege of knowing him as a friend. Elsewhere, I might do this on the grounds that there is no praise so impressive as that which comes at second hand. Here it would be unbecoming to do more than thank his friends who have given me a valued picture of Dr. Banting's inspiring qualities.

The other tribute is to recall Banting's contribution to the lives and work of many physicians and investigators. In the soil prepared by Langerhans, Minkowski and many others, Banting and his associate Best planted a great tree. This symbolism is used to suggest the growth, spread and ramification of their work. The trunk of this tree is insulin and the 28 rings which would show its age typify the ever expanding number of diabetics who are enjoying useful life because of insulin. This is the solid lumber which the public appreciates. Physicians add to this an appreciation of some of the larger branches, the more important of which are as follows. Appearing about 1924 was the branch which represents hypoglycæmia. It takes a sizeable chapter in medicine to describe this one outgrowth of the discovery of insulin. Intertwined with this, is another large branch called insulin sensitivity. From this arises the work of Houssay which resulted from his observation of the insulin sensitivity of hypophysectomized animals. Growing close to this is another large branch—insulin resistance. This has smaller branches representing a number of clinical, immunological and physiological developments. A somewhat irregular branch marks the slow, erratic development of certain details of the clinical use of insulin. Bending in different directions, it is not yet clear which way it will finally grow. Thus far it has not contributed much to the sturdy trunk of the tree. Ten to fifteen years later there appeared an unexpected branch which may be labelled "arteriosclerosis in spite of insulin treatment". Finally, the actively growing top of the tree with countless small branches may be used to indicate the unknown mechanism of action of insulin, and the complex studies related thereto.

Banting accomplished much. With his associates, he proved the existence of insulin and obtained it in a potent, non-toxic form. The life span of the diabetic was increased. But with these achievements, a host of questions were raised, all based on the fact that insulin was available. This enduring stimulus to the work, thought, and lives of men is Banting's living memorial.

As a small part of the structure that has developed since the discovery of insulin, I shall report three recent studies of our laboratory. All are related to the pathogenesis of diabetes but this topic as a whole is too large to review. I must call attention to the fact that the experiments cited comprise only a part of our knowledge of the pathogenesis of diabetes.

The first investigation concerns the relation of insulin and pituitary growth hormone. Since Dr. Young spoke here last year, it is enough to recall the production of experimental diabetes by means of crude pituitary extract by Young,[1] Campbell and Best[2] and others, and the recent production of diabetes by Cotes, Reid and Young,[3] Campbell, Davidson and Lei[4] and Houssay[5] by highly purified growth hormone. These results highlight the diabetogenic action of growth hormone. In addition to the production of diabetes, the anti-insulin effect of growth hormone has been examined in dogs[6, 7] and rats.[8] Stadie, Haugaard, Hills and Marsh[9, 10] and Park and Krahl[11] have observed the inhibition of insulin action upon the rat diaphragm *in vitro*. Drs. Milman and DeMoor in our laboratory measured the relation between insulin and growth hormone in terms of nitrogen retention. These four effects of growth hormone, namely, diabetogenic activity; insulin-resistance; nitrogen retention; and the inhibition of insulin *in* vitro may be briefly reviewed. The diabetogenic effect has been well established. Since Dr. Young addressed you last year, I need only say that we have confirmed this effect by the incidental finding of glycosuria in some of our animals given growth hormone.

By giving growth hormone to hypophysectomized dogs, deBodo[6, 7] abolished their sensi-

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The Eighth Banting Memorial Lecture, delivered in Toronto on February 21, 1951. This was also the occasion for the unveiling by Professor C. H. Best of a bust of Sir Frederick. The bust stands in Simcoe Hall.

tivity to insulin in 2 to 4 days. With more prolonged administration, insulin resistance and in some instances diabetic glucose tolerance curves were produced.[7] In these results, growth hormone has a contra-insulin effect of great range since it transformed marked insulin sensitivity to diabetes. The rôle of time in the action of growth hormone is also clarified. The duration of its administration is perhaps more important than the daily dosage in milligrams. This may be one reason why growth hormone is ineffective when added to tissues *in vitro*, although it inhibits the combination of insulin with the diaphragms of pretreated animals.[9, 10, 11]

The effect of growth hormone upon the retention of nitrogen in various types of insulin deficiency has been the subject of many investigations.[8, 12, 13] These experiments have not included total insulin deficiency and in the older ones pure growth hormone was not available. The purified growth hormone has been generously provided by the Armour Laboratories. This has been tested for its effect on nitrogen balance in totally depancreatized cats on constant or experimentally adjusted insulin dosage and in "Houssay" cats receiving no insulin. By these means it has been possible to treat depancreatized cats with doses of insulin ranging from none to several times the usual maintenance dose. Under this varied supply of insulin the nitrogen retaining effect of growth hormone varied respectively, from zero to the amount observed in normal cats.

When depancreatized cats which were given a constant diet and dose of insulin were treated with growth hormone, their average nitrogen excretion decreased. In Table I, the difference

TABLE I.

NITROGEN RETAINING EFFECT OF GROWTH HORMONE (GH)
3 mgm. GH daily for 4 to 6 days

No. of cats	*Average nitrogen excreted*		*Nitrogen retained*
	Control period	*GH period*	
	gm./day	*gm./day*	*gm./day*
5 N*	5.0 ± 0.02	4.1 ± 0.11	0.9 ± 0.08
5 D	6.1 ± 0.3	5.9 ± 0.3	0.2 ± 0.04

*N—normal; D—depancreatized.
Diet and insulin were constant for each cat.

between the urinary nitrogen excreted during the control periods and during the subsequent periods of treatment with growth hormone is recorded in the last column as the average amount of nitrogen retained. These studies show that when the supply of insulin was constant nitrogen was stored under the influence of growth hormone. However, the amount of this storage was less than that of normal animals treated in a similar manner, a result supporting the concept that insulin is normally secreted in response to growth hormone. Gaebler[12] obtained similar results using single doses of growth hormone instead of the longer metabolic periods used in our cats. Growth hormone increased the glycosuria of animals on a fixed dose of insulin and this was probably a significant factor in the impaired nitrogen retention. The fall in the blood sugar of fasted normal animals, which has been reviewed and confirmed,[8] also supports the concept of insulin secretion in response to growth hormone.

In two depancreatized cats the effect of increasing the dose of insulin was investigated. As a control observation we determined that under the conditions employed, the largest increments in insulin alone that could be given without producing hypoglycæmia caused no storage of nitrogen. This confirmed the fact, established after the discovery of insulin, that although insulin counteracts the protein catabolism of diabetic acidosis, it does not cause storage of nitrogen in normal animals or in reasonably controlled diabetics. With this background the influence of progressively larger doses of insulin on the anabolic action of growth hormone was examined. Fig. 1 shows the results of the con-

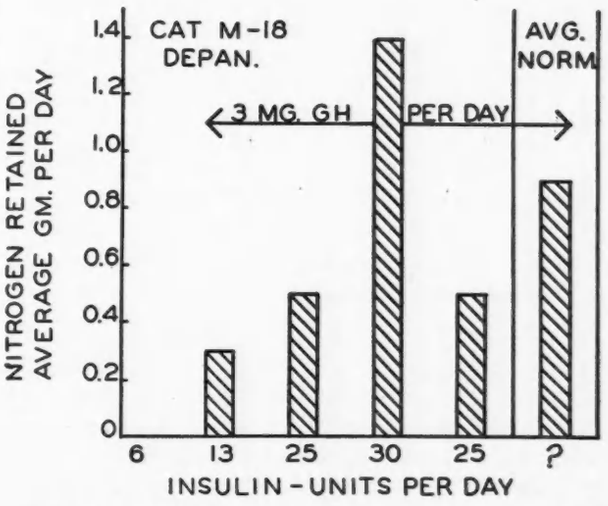

Fig. 1. Cat M-18.— This animal was depancreatized and after recovery was maintained on a constant diet throughout all periods charted. Each column represents the average nitrogen retained during consecutive 3 to 5-day metabolic periods. The retention of nitrogen has been measured by the decrease in its excretion from the control period on 6 units of insulin daily before the administration of growth hormone. For comparison the average of 5 normal cats tested for similar metabolic periods is shown in the last column.

secutive metabolic periods in one of the animals so studied. The results were similar in the other animal. Both showed that by increasing the dose of insulin three- to five-fold the normal degree of nitrogen retention occurs. This provides an approximation of the stress placed upon the islands of Langerhans by the action of the single dose of growth hormone tested.

Since the average survival of untreated depancreatized cats is 3 days, adequate control and treatment periods without insulin would be impossible. We therefore prepared depancreatized-hypophysectomized cats which could be stabilized on a constant diet without insulin. Growth hormone was given to three such animals. Fig. 2 illustrates the response seen in

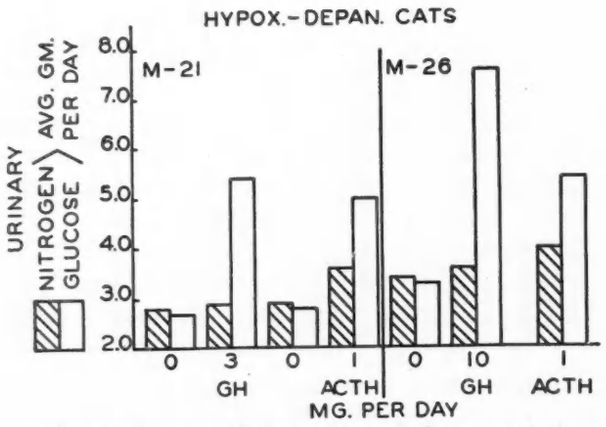

Fig. 2.—The average excretion of glucose and nitrogen (3-day periods) of hypophysectomized-depancreatized cats receiving no insulin. The nitrogen excretion was not decreased by growth hormone (GH) as it was in depancreatized cats given insulin (*cf.* Fig. 1). On the other hand, ACTH significantly *increased* the nitrogen excretion. The common action of both hormones in increasing glycosuria is presumably effected by different mechanisms. The results indicate that insulin is essential for the anabolic action of growth hormone.

two of these animals. In the absence of insulin growth hormone failed to cause nitrogen retention. This is not attributed to the increased glycosuria since the glycosuria in these animals was less than in many of the depancreatized cats on fixed doses of insulin. The fact that the glycosuria was increased in these cats indicates that in these experiments this effect of the hormone occurred by an action elsewhere than on the pituitary or the pancreas. The results thus support the evidence obtained from eviscerated animals[14] and isolated tissues that much if not all of the action of growth hormone on carbohydrate metabolism takes place in the tissues (muscle).

Because ACTH is also diabetogenic[15] it was tested in these animals (Fig. 2). In the dose tested, ACTH produced a degree of glycosuria similar to that of growth hormone, but unlike growth hormone, ACTH caused an increased excretion of nitrogen. It is known that under other conditions, ACTH increases glycosuria out of proportion to the change in nitrogen excretion by some mechanism other than gluconeogenesis from protein, so that the results which seem to distinguish ACTH and growth hormone so clearly in these Houssay animals do not account for all the facts.

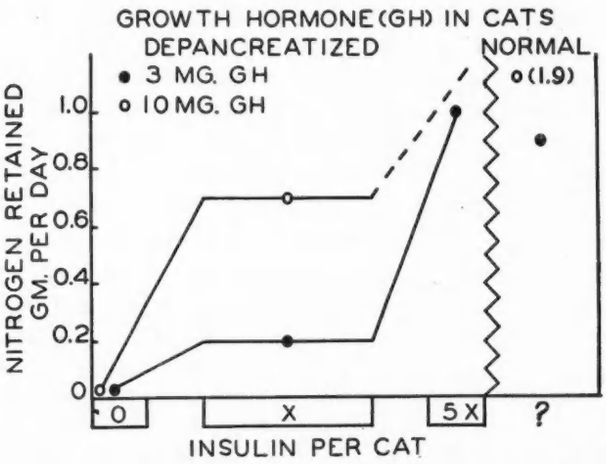

Fig. 3.—Schematic summary of the relation between growth hormone and insulin, as measured by the retention of nitrogen. O refers to the absence of nitrogen storage in hypophysectomized-depancreatized cats without insulin (*cf.* Fig. 2). X insulin per cat refers to the fixed maintenance dose of insulin during control and growth hormone (GH) periods. 5X indicates the increase above the maintenance dose of insulin which restores the nitrogen retaining action of GH to normal (Fig. 1). For the 10 mgm. dose of GH this point was not determined and the broken line suggests an anticipated response. Average normal values are given for comparison.

Fig. 3 summarizes the results of our studies on nitrogen metabolism in schematic form. It shows that without insulin there is no storage of nitrogen. At constant insulin dosage some storage of nitrogen occurs which is much less than normal. If insulin is increased by three to five-fold the retention of nitrogen reaches the normal level. When insulin is present, in either restricted or normal amount, 10 milligrams of growth hormone causes a greater anabolic effect than 3 milligrams.

When these results are related to previous studies the picture appears to be somewhat as follows. Growth hormone causes insulin resistance but at the same time leads to an increased secretion of insulin which prevents glycosuria and facilitates the storage of nitrogen. It seems that for optimal protein anabolism a special

equilibrium between these hormones is required. Since the glycosuria and anti-insulin effects of growth hormone can occur without the pituitary, pancreas or liver and since their interference with insulin is also demonstrable upon muscle *in vitro*, it appears that most of the anti-insulin effect is exerted on the tissues. In the tissues, growth hormone acts not on the insulin molecule but on the anatomical or chemical site of insulin action.

Turning to speculation, all of the findings might be explained if growth hormone had a relatively greater anti-insulin effect on adipose tissue, or fat formation, than on carbohydrate metabolism in general. The same result might be due to a difference in the effect of insulin on adipose and muscle tissue, since the question is one of the equilibrium between these hormones. The influence of growth hormone upon fat metabolism is well recognized although it is impossible to say whether this is exerted directly or indirectly. Under some conditions growth hormone and ACTH are ketogenic[16] and both may mobilize fat from the depots to the liver.[17] However, only growth hormone spares protein at the expense of fat as demonstrated by carcass analysis.[18] This utilization of fat has been found in rats, which do not develop diabetes and in which there is a probable increase in insulin production. Therefore, this increased insulin production does not prevent the increased utilization of fat although it maintains essential carbohydrate metabolism, prevents diabetes and promotes optimal storage of nitrogen. At present such speculation merely points to problems which must be solved by further research.

In any case the need for as much as five times the maintenance amount of insulin to support the action of growth hormone, shown by Gaebler[12] and by these studies, affords an elementary explanation of why growth hormone is diabetogenic.

With any diabetogenic pituitary extract, the first effects are physiological changes which lead to hyperglycæmia and glycosuria. If this abnormality is maintained, damage of the islands of Langerhans ultimately follows. At first the lesions are reversible but later they become irreversible so that the permanent phase of the diabetes is pancreatic. Since the Toronto investigators have contributed so greatly to this subject further introduction is superfluous. It is in connection with this problem that Dr. Dohan and I have studied the possible rôle of hyperglycæmia as a cause of the island damage. During the past 10 years we have made three general observations. (a) The control of pituitary-diabetes in cats by insulin[19] led to the prevention of lesions of the islands or to their recovery provided the lesions had not progressed to atrophy. (b) The same results were observed when the hyperglycæmia was controlled with phlorhizin.[20] (c) The complete cycle of island lesions which had previously been described after partial pancreatectomy or pituitary extract, was produced by the administration of massive quantities of glucose.[21] In the glucose experiments, cats were used and the glucose was administered intra-peritoneally every eight hours. If the injections of glucose did not produce *sustained* hyperglycæmia there were no lesions of the islands. If sustained hyperglycæmia was maintained for 2 weeks or more the islands showed marked hydropic degeneration, and in a few instances this was continued for 6 weeks or more causing permanent diabetes like that produced by pituitary extract.

These results led us to try further experiments in the dog, since the dog was a species susceptible to pituitary extract. Intraperitoneal administration of glucose failed to raise the blood sugar level in the dog and the intravenous administration had been unsuccessful as reported by others. Drs. Brown, Freedman and DeMoor then attempted the perfusion of the pancreatic arteries of dogs with glucose. After many technical difficulties it was possible to infuse 5 to 17% glucose in the common hepatic artery for periods as long as three weeks. We had hoped to produce lesions of the islands in the infused portion of the pancreas while the splenic portion served as a control. This was not accomplished, probably due to the free collateral circulation of the pancreas. It is true that the supposedly non-infused portions were histologically normal. We also found that the infused portions of the pancreas were normal, or showed hypertrophy of the islands, or degranulation of the beta cells. These are the three possibilities that one would expect when collateral circulation completely protected or permitted stimulation or permitted minimal stress of the islands. Regardless of whether hypertrophy was seen or not, there was physio-

logical evidence of the stimulation of insulin secretion by the infused glucose. When the common hepatic artery was infused the peripheral blood glucose fell to hypoglycæmic levels. In some cases it remained in the thirties (30 to 40 mgm. per 100 ml.) for as long as two weeks; in one case the animal died of hypoglycæmic convulsions while concentrated glucose was entering the arterial system. The common hepatic artery sends branches to both the pancreas and the liver. In order to exclude the liver as a factor in this phenomenon, a few experiments were added in which the portal vein was perfused. In these cases the peripheral blood sugar remained normal. The contrast was definite and showed that the perfusion of the pancreas with glucose in this manner leads to a prolonged and marked hypoglycæmia. Physicians are familiar with this in the "undershoot" of the normal glucose tolerance curve. Physiologists have described the phenomenon in brief experiments but I know of no such sustained demonstration of the action of glucose as a stimulator of insulin secretion.

When this evidence for glucose as a stimulant of insulin secretion is combined with previous studies on the rôle of hyperglycæmia as a factor in the pathogenesis of experimental lesions, it seems clear that hyperglycæmia is one element with which we must reckon. It is obvious that these studies do not exclude other elements in the pathogenesis of island damage. Finally I may point out one practical implication based on the administration of glucose to cats. If the blood sugar is normal once or twice a day, the animals will not develop lesions of the islands. This suggests that good practical control of early human diabetes may be worth while. I might add that, by analogy, no amount of the usual tolerance tests or parenteral glucose therapy could be harmful to the islands.

The third topic is the biochemistry of alloxan, which cannot be related to the studies just described. Suggestions have been made in the literature that alloxan might be related to the pathogenesis of human diabetes. The concept that alloxan might be produced from uric acid in the body[22] has received indirect support from the findings of Griffiths[23] that massive doses of uric acid were diabetogenic. Other investigators have studied certain chemical and physiological relations between alloxan and sulfhydryl compounds.[24] However, only a few of these studies have been directed toward the fate of alloxan in the body. It has been amply demonstrated, that alloxan is quite unstable and disappears as such in a few minutes when exposed to biological fluids. However, the end products of the breakdown of alloxan have not been established. During the past year Dr. Seligson has developed methods applicable to this problem. The conversion of alloxan to alloxanic acid or its salts, alloxanates, was described by earlier workers. By a series of oxidative and hydrolytic reactions not previously applied to this reaction, Dr. Seligson has found that this conversion occurs in plasma. Alloxanic acid is difficult to identify, but on hydrolysis in hot alkali it breaks down to form the 3-carbon moiety, oxomalonic (mesoxalic) acid. A simple colorimetric method for the determination of microgram quantities of oxomalonic acid has been developed. Thus far, no other precursors than alloxan or alloxanic acid have been found to yield oxomalonic acid after hydrolysis but it is too soon to claim that the reaction is specific.

Efforts are being made to apply these methods to urine. By means of solvent and chromatographic separations, a fraction has been extracted from urine which presumably contains alloxanic acid. One item of evidence for this is the recovery of 50% or more of added alloxanate, the recovery being made by hydrolysis and measurement as oxomalonate. The quantitative accuracy of these methods, when applied to urine, requires further improvement. Even so, urine samples from 15 persons, normal and diabetic, contained oxomalonic acid in varying amounts. This work is continuing on the provisional assumption that the oxomalonate comes from a substance yielding alloxanate and that alloxanate can come only from alloxan. It will take much more study to determine whether alloxan is, or is not, related to human diabetes but we believe that the problem will be attacked on a broader front if the conversion of alloxan to the relatively stable alloxanic acid is made part of the campaign.

In closing I should repeat that these observations are but three leaves on the tree that has grown since the discovery of insulin. If these small examples help to illustrate the course of events since then and if they are later incorporated in the structure begun by Banting, my associates and I have rendered our small tribute to his inspiring memory.

REFERENCES

1. YOUNG, F. G.: *Lancet*, **2**: 372, 1937.
2. CAMPBELL, J. AND BEST, C. H.: *Lancet*, **1**: 1446, 1938.
3. COTES, P. M., REID, E. AND YOUNG, F. G.: *Nature*, **164**: 209, 1949.
4. CAMPBELL, J., DAVIDSON, I. W. F. AND LEI, H. P.: *Endocrinology*, **46**: 588, 1950.
5. HOUSSAY, B. A. AND ANDERSON, E.: *Endocrinology*, **45**: 627, 1949.
6. DEBODO, R. C., KURTZ, M., ANCOWITZ, A. AND KIANG, S. P.: *Am. J. Physiol*, **163**: 310, 1950.
7. *Idem*: *Proc. Soc. Exper. Biol. & Med.*, **74**: 524, 1950.
8. MILMAN, A. E. AND RUSSELL, J. A.: *Endocrinology*, **47**: 114, 1950.
9. STADIE, W. C., HAUGAARD, N., MARSH, J. B. AND HILLS, A. G.: *Am. J. M. Sc.*, **218**: 265, 1949.
10. STADIE, W. C., HAUGAARD, N., HILLS, A. G. AND MARSH, J. B.: *Am. J. M. Sc.*, **218**: 275, 1949.
11. PARK, C. R. AND KRAHL, M. E.: *J. Biol. Chem.*, **181**: 247, 1949.
12. GAEBLER, O. H. AND ROBINSON, A. R.: *Endocrinology*, **30**: 627, 1942.
13. BENNETT, L. L. AND LAUNDRIE, B.: *Am. J. Physiol.*, **155**: 18, 1948.
14. RUSSELL, J. A.: *Am. J. Physiol.*, **140**: 98, 1943.
15. INGLE, D. J., WINTER, H. A., LI, C. H. AND EVANS, H. M.: *Science*, **101**: 671, 1945.
16. BENNETT, L. L., KREIS, R. E., LI, C. H. AND EVANS, H. M.: *Am. J. Physiol.*, **152**: 210, 1948.
17. LI, C. H., SIMPSON, M. E. AND EVANS, H. M.: *Arch. Biochem.*, **23**: 51, 1949.
18. *Idem*: *Endocrinology*, **44**: 71, 1949.
19. LUKENS, F. D. W. AND DOHAN, F. C.: *Endocrinology*, **30**: 175, 1942.
20. LUKENS, F. D. W., DOHAN, F. C. AND WOLCOTT, M. W.: *Endocrinology*, **32**: 475, 1943.
21. DOHAN, F. C. AND LUKENS, F. D. W.: *Endocrinology*, **42**: 244, 1948.
22. DUNN, J. S., SHEEHAN, H. L. AND MCLETCHIE, N. G. B.: *Lancet*, **1**: 484, 1943.
23. GRIFFITHS, M.: *J. Biol. Chem.*, **184**: 289, 1950.
24. LAZAROW, A.: *Physiol. Rev.*, **29**: 48, 1949.

FIBROSITIC HEADACHE

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ALTHOUGH headache is probably the most common of all human ailments, in most textbooks of medicine the subject is rather sketchily treated. Several investigators, notably Wolff[1] and his co-workers have devoted much effort to the study of pain in general and head pain in particular; but it may be said that the average practitioner, when confronted with headache which is persistent, does not respond to the usual analgesics, and is not associated with grossly abnormal physical signs, frequently finds himself at a loss for a diagnosis. Excluding well-documented entities such as migraine, meningitis and expanding intracranial lesions, headaches are usually ascribed to constipation, errors of refraction, dental caries, and other less clearly-defined abnormalities. If all these actual and presumed causes of headache have been satisfactorily excluded, it is sometimes extremely difficult to classify etiologically certain persistent headaches which are occasionally encountered by general practitioners and specialists alike.

The purpose of this communication is to emphasize the existence of a specific type of headache, which can readily be recognized on physical examination alone and treated in a simple manner, usually with permanent and excellent results. I refer to the condition known as "fibrositic headache" or headache due to fibrositis of the scalp muscles and their attachments. This syndrome must be distinctly more common than is generally appreciated since, during the past year, three unmistakable cases have been diagnosed and treated in the population of a hospital devoted to the management of pulmonary tuberculosis. The occurrence of this number of cases in so select a group suggests that it must be even more common in the general population; and this leads to the assumption that there must be many persons with long-standing persistent headache which could probably have been diagnosed and treated satisfactorily if the symptom-complex were more generally recognized.

It is of some interest that, in recent years, the occurrence of fibrositis in other sites has received considerable attention. Much has been written during this period regarding low-back pain, shoulder pain, and pain in the chest muscles with this etiology. But it is indeed somewhat surprising that the general interest in the fibrositic state has apparently not extended to the scalp, in spite of the probable frequent occurrence of persistent undiagnosed and untreated headache.

Studies in this direction have received a degree of impetus as the result of the work of Weiss and Davis,[2] and Travell and Rinzler,[3] on the concept of somatic trigger zones. But even these workers have confined themselves to the elucidation of the mechanism of somatic trigger areas resulting from *visceral* disease, particularly involving the heart, and have not, to date at least, extended their studies to the mechanism of headache.

Since the work of Travell and Rinzler has an important bearing on the subject of this paper, a brief outline of their concepts is probably indicated.

According to Travell, a "somatic trigger zone" is a discrete area, located either in the

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skin or within myofascial structures, which, so far as is known at present, develops spontaneously and is not yet reproduceable experimentally. Such an area, hypersensitive to pressure, produces referred pain, nearby or distant, constant or intermittent. It is believed to initiate a self-sustaining or autogenic cycle of nerve impulses, this characteristic being considered responsible for the persistent character of the referred pain. A somatic trigger area may be rendered *permanently* inexcitable by local blocking agents which have *transitory* pharmacologic actions, such as ethyl chloride or procaine. It is the interruption of the aforementioned autogenic cycle of impulses which is apparently responsible for the prolonged relief of pain afforded by local blocking.

A somatic trigger area may be initiated or activated by a wide variety of causes including local trauma, chilling, ischæmia, or infection and, in the case of visceral structures, by infarction, inflammation or mechanical distension.

The investigations carried out by Travell and Rinzler[4, 5] on this subject have been confined chiefly to the diagnosis and treatment of pain due to somatic trigger zones following myocardial infarction or skeletal trauma, and they have reported satisfactory results from the use of ethyl chloride spraying and procaine.

The material on which this paper is based is somewhat far removed from, though bearing certain resemblances to, visceral referred pain. My interest in this subject was stimulated by the occurrence of a rather standardized type of headache occurring in the population of a tuberculosis sanatorium. It is obvious that, in a 200-bed institution for the treatment of any chronic disease, large numbers of headaches will occur, most of which never reach the notice of the attending physician. However, in an institution for the treatment of tuberculosis, the symptom of headache assumes a somewhat magnified importance, because of the constant vigilance required for the detection of incipient cases of tuberculous meningitis. Therefore, in this institution, it is a matter of routine that all headaches persisting for longer than 48 hours, and unrelieved by the usual analgesic drugs, are brought to the notice of the attending physician. If indicated, spinal puncture is then performed and tuberculous meningitis is ruled out. If the latter disease has been satisfactorily excluded, a search is made for other causes of headache, including errors of refraction, sinus disease, migraine, etc. It has been our experience that, when all these conditions have been excluded, the cause of persistent headache is usually found to be the presence of a somatic trigger zone in the myofascial structures of the scalp, based on fibrositis.

There are certain consistent features of this type of headache, which should lead to the correct diagnosis, even when all other causes of headache have not yet been excluded. These are as follows:

1. The headache is usually severe. It is not uncommon to receive a report that, in the case of a female patient, it is of sufficient severity to make the patient weep.

2. It does not respond to the usual simple analgesic preparations.

3. It is not usually frontal in distribution, but is frequently occipital, or cannot be localized.

4. It is not usually throbbing in character, as are many headaches, but the patient frequently complains of a "sore head" rather than a headache.

5. Finger palpation reveals the presence of tender areas in the scalp, and frequently tender superficial nodules are encountered.

6. These tender areas or nodules are most frequently distributed at the insertion of the posterior neck muscles into the superior nuchal line of the skull, but may be found anywhere in the scalp.

7. Firm pressure on these tender areas or nodules produces shooting pains in the head, usually reproducing the described characteristics of the headache, and results in the reappearance and persistence of the headache for a more or less prolonged period of time.

8. Pinching of the free borders of the cervical portions of the trapezius muscles frequently causes more pain than would normally result from such a manœuvre, and nodules can occasionally be felt within these borders.

The similarity of these findings to those noted in previous descriptions of somatic trigger zones led us to attempt to inactivate these tender areas, which we believed to be counterparts of such trigger zones, or actual trigger zones in an unusual site. Local block with procaine was therefore carried out in the illustrative cases reported below.

CASE 1

R.M. This subject was a 22 year old white female, who had been a patient in Point Edward Hospital for

several months, suffering from moderately advanced pulmonary tuberculosis. She had been treated on a regimen of modified bed rest, supplemented by right artificial pneumothorax. During her treatment at this hospital, she suddenly began to complain of "pain in the back of the head". History and physical examination revealed no evidence of migraine, errors of refraction, sinus disease, or any other of the usual causes of headache. Spinal puncture ruled out tuberculous meningitis. Careful palpation of the scalp revealed several tender areas and a few nodules, mainly grouped about the insertion of the posterior neck muscles into the superior nuchal line, but also scattered through other areas of the scalp. Pressure on these tender areas and nodules reproduced and accentuated the headache. All these tender areas and nodules were marked, and were injected with 1% procaine, a total of 10 c.c. procaine being used. At the conclusion of this procedure, the patient stated that her headache had completely disappeared, and there was no recurrence.

CASE 2

C.B. This was a 19 year old white female suffering from far advanced bilateral pulmonary tuberculosis, treated by bed rest. She complained of a severe occipital headache, which had been treated by the nursing staff on the ward with the usual analgesic preparations for 48 hours, before being reported to the attending physician. Little or no relief had been afforded by these measures. History and physical examination revealed no evidence of migraine, errors of refraction, sinus disease, or any other of the usual causes of headache. Spinal puncture was carried out, and the cerebrospinal fluid was normal in all respects. Careful examination of the scalp revealed numerous circumscribed areas of deep tenderness, mostly in the occipital region, with a single tender nodule in the mid-line at the vertex. There was also excessive tenderness on pinching the anterior borders of both trapezii. Injection of these tender areas with 1% procaine resulted in dramatic and complete relief of headache without recurrence.

CASE 3

M.J. An 18 year old Indian girl with moderately advanced pulmonary tuberculosis, complained of severe generalized headache, which had lasted for three days, without relief from aspirin. Her vision had recently been tested, and she had been wearing new glasses for the past several months. Investigation revealed no evidence of migraine or other syndrome, and tuberculous meningitis was ruled out by spinal fluid examination. Careful palpation of the scalp revealed a half-dozen tender areas, pressure on which reproduced and accentuated her symptoms, but no nodules were found. Injection of these tender areas with 1% procaine resulted in complete and dramatic relief of the headache, which did not recur.

The most striking feature of these three illustrative cases was the rapidity and completeness with which the symptoms responded to the local injection of 1% procaine. In all cases, it was most gratifying to note that patients who had been suffering from severe headache for several days were completely relieved by this simple procedure, and that symptoms did not recur in any case. I had noted similar gratifying relief of pain in the treatment of lumbar fibrositis by this method, and, as indicated above, similar methods have been employed by other workers in the treatment of cutaneous manifestations of visceral pain. It seems quite reasonable to suppose that lumbar fibrositis, somatic trigger zones, and this syndrome, which we have called "fibrositic headache" are all variations on a similar theme. In lumbar fibrositis and in fibrositic headache the lesion and the trigger zone are one and the same, while in the case of true trigger zones, the lesion is visceral and the somatic manifestation is a referred phenomenon. In any case, treatment of the local accessible area by inactivation with procaine produces satisfactory results in both types of cases.

The theoretical explanation of this syndrome, and the form of treatment, as advocated in other sites, are not new. Mount[6] has recently described cases of atypical facial and head pain, in which trigger areas were inactivated, first by procaine injection, and later, permanently, by periarterial sympathectomy. It is my purpose merely to call attention again to the fact that such an occasionally vague syndrome as headache can be produced by a well-known pathological process, and can be treated in the same way as similar pathological processes in different sites. The only new feature of this presentation is the recommendation that the syndrome be more frequently recognized. Such recognition of a symptom-complex involves only a knowledge of its existence, and a high index of suspicion as to its presence. Once the diagnosis has been made, treatment follows naturally and is usually attended by dramatically successful results.

SUMMARY

1. A rarely-recognized syndrome, termed "fibrositic headache", is described.

2. The theoretical background of this form of headache is outlined, and its similarity to the well-known manifestation of "somatic trigger zones" is suggested.

3. The detailed symptomatology of fibrositic headache is presented, and a successful form of treatment, namely local procaine block, is recommended.

4. Illustrative cases are described.

REFERENCES

1. WOLFF, H. G.: Headache and Other Head Pain, Oxford University Press, New York, 1948.
2. WEISS, S. AND DAVIS, D.: *Am. J. M. Sc.*, **176**: 517, 1928.
3. TRAVELL, J., RINZLER, S. AND HERMAN, M.: *J. A. M. A.*, **120**: 417, 1942.
4. TRAVELL, J. AND RINZLER, S. H.: *Proc. Soc. Exper. Biol. & Med.*, **63**: 480, 1946.
5. RINZLER, S. H.: *Am. J. Med.*, **5**: 736, 1948.
6. MOUNT, H. T. R.: *Canad. M. A. J.*, **64**: 131, 1951.

Point Edward Hospital,
March 15, 1951.

INFANTILE SPINAL PROGRESSIVE MUSCULAR ATROPHY IN TWINS

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Edmonton, Alta.

PROGRESSIVE muscular atrophy in infancy was first described in 1892 by Werdnig and later by Hoffman. Almost all the cases described, about 30 in number at that time, occurred in several children of the same family: the disease could be traced through two or three generations. In typical cases there is degeneration of the anterior horn cells in the entire spinal cord, degeneration of the root fibres and of the motor nerves. The white matter of the spinal cord and the brain remain quite normal. The muscles show merely secondary atrophy.

This heredo-familial disease is usually noticed for the first time between 6 months and 12 months of age. If the infant is followed closely, it may be seen that the weakness begins in the gluteals and other muscles about the hips, slowly extending into the lumbar regions, shoulders, thighs, upper arms, legs and forearms. The fingers and toes are usually not involved at the beginning. Later, intercostal and abdominal muscles become involved and breathing is diaphragmatic. The paralytic muscles lose their tone, distorted posture results and secondary fibrous contractures develop. Tendon reflexes are slowly lost. There is no pain or other sensory disturbance. The mental condition is not affected and sphincter control is not lost. Bulbar palsy has been described but is exceptional.

The muscles will not react to faradic or galvanic currents but in some cases, the galvanic response is preserved and only the faradic is lost: this is called the reaction of degeneration and indicates that the muscular atrophy is secondary to injury to the lower motor neurons.

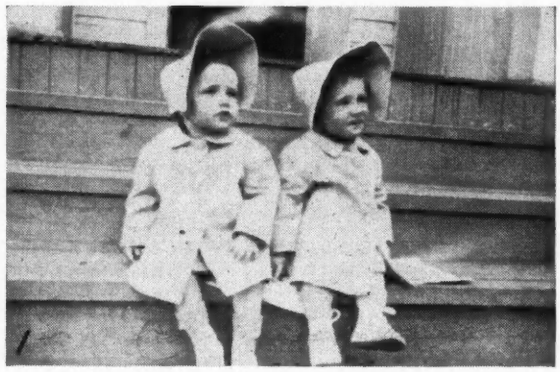
The course is slowly progressive and death usually occurs within five years: there is no remission and no treatment.

CASE REPORT

Judith H. and Janice H., identical twins, were born prematurely on February 5, 1945 weighing respectively 5 lb. 5 oz. and 5 lb. 1 oz. Labour and delivery were uneventful. They progressed normally during the newborn period.

During the first semester they appeared quite normal, taking feedings well, gaining weight and appearing alert. At 9 months of age they could sit up with assistance (they never were able to sit up without assistance). They never crept or walked although at 18 months of age, they could use a walker. At that age they were saying many words, had no difficulty in swallowing and were mentally alert. At 12 months, each child weighed about 20 pounds.

The parents noticed no abnormality until the twins were 14 months of age: at that time they had "red measles". Following this illness it was noticed that their extremities (lower first) were becoming weaker. They would "stiffen" whenever they were frightened. Several doctors were consulted and a diagnosis of "muscular dystrophy" was made. Ever since then, the parents have noticed that their condition has become progressively worse. Firstly, they lost the use of the lower extremities and the muscles became atrophic. At the age of 3 years, the upper extremities were involved with loss of muscle tone.



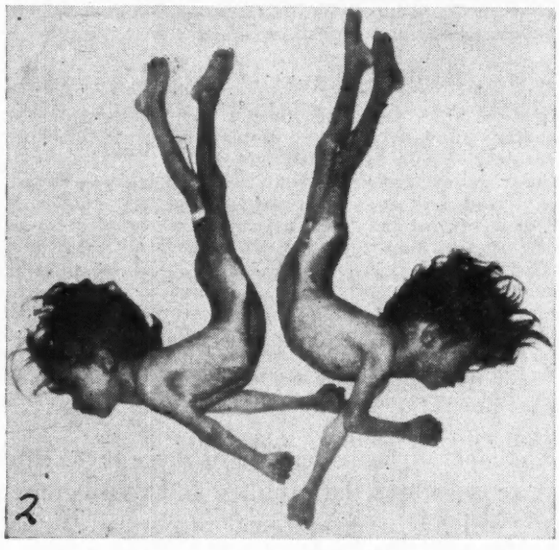


Fig. 1.—At age of 17 months. **Fig. 2.**—At 6 years. Weight 20 lb., 12 oz. and 20 lb., respectively.

For the past 2 years they have been spastic, lying motionless in opisthotonos: when picked up for feeding, they can be brought into a sitting position and will remain in that position, fairly well relaxed for the entire feeding. Strained foods and fluids are given by spoon.

They have been suffering with severe constipation: suppositories have been used daily with digital removal of the stool. They appear to have bladder control but it has been difficult for them to express their need.

The parents have made every effort to try to trace any similar illness in the family but none could be found.

Examination revealed emaciated, twin females, weighing 20 lb. and 20 lb. 12 oz. respectively (no gain since

they were 12 months old). They are very spastic, assuming a constant opisthotonos position and remaining motionless throughout the examination. No discomfort or sign of pain was noticed. Extensive and generalized atrophy of all muscles was present.

Their measurements showed that the skeletal growth had not been affected as much as the musculature. Due to spasticity, reflexes could not be obtained although even when relaxed in a sitting position, no reflexes could be elicited.

Examination of eyes, eardrums and nasal mucosæ revealed no abnormality. Pharynx was filled with saliva and secretions but there was no evidence of paralysis of the palate. Neck was rigid and could not be moved forward. Heart and lungs were normal. Respiration was diaphragmatic. Spleen was not palpable and liver was not enlarged. Abdominal reflexes were absent. Spine was in opisthotonos position and the limbs were held in complete extension; no reflexes were present; toes and fingers were moved occasionally; Babinsky was present; all muscles of extremities were atrophic. Skin was well hydrated but very little subcutaneous fat could be palpated.

Laboratory investigation gave fairly similar reports in both children. Urinalysis, red blood count, leucocyte count and hæmoglobin were normal. Urinary creatinine was markedly elevated, having a daily creatine excretion of 930 mgm. for Judith and 730 mgm. for Janice. Sedimentation rate was within normal limit at 5 mm. and 6 mm. respectively. Wassermann and Mantoux tests were both negative.

During this investigation, ACTH was given to one of the children: the eosinophile count dropped very rapidly but there was no change noticed in the condition and treatment was resumed after one week.

BIBLIOGRAPHY

1. BRENNEMAN'S: *Practice of Pediatrics*, 4: CL. 16, p. 6, 1948.
2. COMBY: Traité des Maladies de l'enfance, p. 636, 1899.
3. PFAUNDLER AND SCHLOSSMANN: The Diseases of Children, 4: 156, 1908.

AMPUTATION FOR ISCHÆMIC ARTERIAL DISEASE OF THE LEG*

Josephus C. Luke, M.D., F.R.C.S.[Eng.& C.]
Montreal, Que.

ONE of the prices paid for the increasing longevity of the general population is an increase in the manifestations of arteriosclerosis obliterans. There is no doubt that one sees a greater frequency of ischæmic feet than formerly, a fact which the records of any general hospital will substantiate. It is a sad commentary on our lack of knowledge of the pathogenesis and prophylaxis of this disease that limbs must be sacrificed in certain cases just at an age when "second childhood" is developing and where this limb is more than ever necessary to keep the individual mobile. Until improvement in our knowledge of the causative factors in arteriosclerosis and Buerger's disease occurs, the loss of part of the leg will be inevitable in certain cases, and it behooves us to make full use of the existing knowledge to try to save as much functioning limb as possible and so to rehabilitate these unfortunate people to the best of our ability.

The routine use of the above knee amputation in such individuals is wrong, such a procedure results in the creation of many unnecessary "wheel chair invalids". With care and proper preoperative evaluation, many of these limbs can be partially preserved, allowing for an increased possibility of again becoming useful citizens. Or again, with proper evaluation, multiple, gradually ascending amputations will be avoided, saving much pain, expense and prolonged disability. As the majority of these cases are cared for by the general surgeon, and, as there is little specific guidance for the determination of an initial correct amputation level, I have considered the subject worthy of discussion.

The conditions leading to sufficient arterial ischæmia to warrant amputation are, in order of frequency: arteriosclerosis obliterans with or without diabetes, Buerger's disease, following arterial emboli, and acute arterial thrombosis. The indications for amputation in ischæmic arterial disease are either frank gangrene of a digit or portion of the foot, pregangrene associated with severe pain, non-healing ulcers of a toe or portion of the foot associated with severe pain, and osteomyelitis of one of the metatarsals or phalanges.

When faced with a case of gangrene involving a portion of the lower limb, it is obvious that the offending dead area must be removed or allowed to demarcate spontaneously. This therapeutic decision can only be arrived at after most careful investigation. Following three weeks of hospitalization, the surgeon should be able to say whether or not conservative therapy will be effective or that amputation is necessary. If amputation is indicated, the most distal level where good healing should occur can be relatively accurately foretold. The

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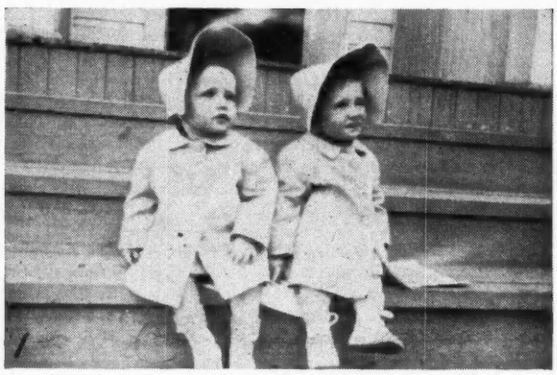

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factors in each case to be ascertained before a proper level can be determined are, in the main, clinical criteria. Inspection and palpation will reveal the majority of detail necessary.

CLINICAL POINTS

1. A foot which shows thin, inelastic, shiny skin and a marked loss of subcutaneous fat is extremely poorly supplied with blood and will not tolerate local amputations. Such a foot has clawlike toes with even worse trophic changes, reduced movements and marked changes in the nails. Rapid ischæmia on elevation and rubor on dependancy will be evident. Paræsthesias are usually present. On the other hand, and despite the level of main artery occlusion, a foot which shows relatively normal skin, good subcutaneous tissue and minimal trophic changes indicates a good collateral circulation and so is more likely to heal following local procedures.

2. It can be said somewhat dogmatically that the presence of either or both of the pedal arteries as functioning vessels will allow healing of a toe amputation when local infection is not a major factor. If the toe to be removed is extensively infected, the amputation wound should be left open to heal by second intention because such wounds, when closed, show a rapid spread of infection due to the relative ischæmia and the local decreased concentration of the antibiotic drugs.

Primary healing of a toe amputation will frequently occur when both pedal arteries are occluded but a good pulsating popliteal is present. However in such a case more detailed study is necessary, as subsequently outlined, to determine this point. A pulsating popliteal will ensure adequate vascularization for healing of a below knee stump and the same applies for a supracondylar amputation when the common femoral artery is functioning. Healing of these latter two amputations can also take place in the absence of the appropriate proximal pulses but here again good preoperative assessment is necessary to determine this fact.

3. A point to bear in mind is the recentness of the arterial occlusion. A leg which has developed arterial ischæmia slowly over a period of many months will, in general, permit a more distal amputation than a similar level of main artery blockage of more recent date. The reason for this is the gradual dilatation of the collaterals when the obstruction is gradual and the lack of such dilatation in the recent occlusion. For example, an arteriosclerotic occlusion of the superficial femoral artery will frequently tolerate successful transmetatarsal or below knee amputation whereas gangrene subsequent to a similarly placed acute thrombosis or embolus invariably requires a supracondylar amputation.

4. In general, it can be said that the degree of arterial occlusion in a case of Buerger's disease which has gone on to gangrene or nonhealing ulceration of a toe is greater than that of arteriosclerosis and consequently local toe amputations have a poorer chance of healing than in similar cases of arteriosclerosis.

5. When infection is present in association with the ischæmic lesion the degree of the inflammatory response will be an aid in assessing the collateral blood supply. A good inflammatory response with redness, heat and swelling indicates a good collateral blood supply despite the level of main arterial occlusion and aids in the opinion that local amputation will be successful. A minimal inflammatory response is a bad prognostic criterion in respect to healing following local amputation.

As can be seen, the finding of a pulsating artery at the various levels is a most important factor in the determination of amputation level and consequently the examiner should be extremely painstaking in this part of the examination. A good rule to go by is to count as absent all pulses where the examiner "thinks" he feels it. Figs. 1, 2 and 3 demonstrate the correct method of palpating the dorsalis pedis, posterior tibial and popliteal arteries. The dorsalis pedis is anatomically absent on the dorsum of the foot in about 14% of normal individuals and, consequently, should be searched for in the anterior ankle region or lower extensor muscle compartment just above the ankle. Where doubt is present after careful examination, the oscillometer will usually indicate whether main artery patency is present or not.

INVESTIGATIONS

The routine adopted in the peripheral vascular service of the Royal Victoria Hospital for the preoperative assessment of these cases is as follows:

1. Careful attention is paid in the history to the length of time the patient has had ischæmic

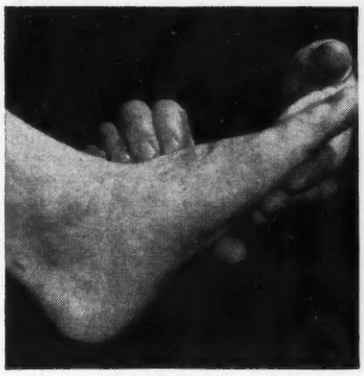

Fig. 1

Fig. 2

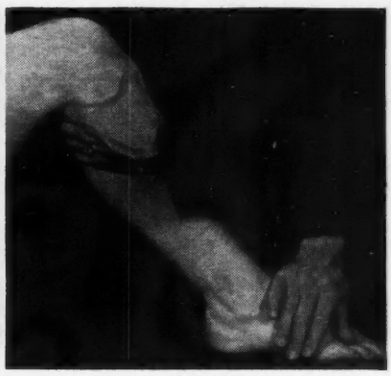

Fig. 3

Fig. 1.—The foot is supported by the left hand and the finger-tips of the right are laid parallel and lateral to the extensor hallucis longus tendon. **Fig. 2.**—The foot is again supported by the examiner's left hand and the ankle flexed almost to a right angle. The finger-tips of the right hand are placed posterior and inferior to the medial malleolus. **Fig. 3.**—The knee is flexed to a right angle with the foot flat so as to relax the soleus and gastrocnemius muscle. The fingers palpate the popliteal space from the lateral side and find the artery just medial to the fibula at the level of the upper end of the tibia.

symptoms and to the initiating cause of the gangrene.

2. The local part of the physical examination is carried out as previously indicated.

3. Urinary and blood sugar examinations are mandatory as diabetes and arteriosclerosis obliterans are so frequently associated.

4. An assessment of the patient's general arterial status can be determined by arterial palpation, determination of femoral and aortic bruits, and examination of the fundi. An electrocardiogram will give some indication of cardiac involvement and x-rays of the thoracic and abdominal aorta, the iliac and femoral arteries will indicate the degree of calcification.

5. Skin temperature readings are taken before and after blockage of the lumbar sympathetic chain to determine the presence or absence of potential vasodilatation of the collaterals. If no rise is obtained after one such block, the test is repeated to rule out technical errors.

6. Oscillometric readings are taken if doubt exists as to main artery patency.

7. Histamine flare tests are placed at the sites of possible amputation namely, base of the toes, midtarsal area, seven inches below the knee, and in the lower third of the thigh. I consider this test to be as good as the intravenous use of fluorescein and simpler to accomplish. The use of radioactive isotopes in the estimation of leg circulation is as yet not practical for a routine test.

ILLUSTRATIVE CASE RECORDS

CASE 1

D.S., aged 58 and diabetic, was admitted with gangrene of the distal phalanx of the left big toe subsequent to an attempt to cut an ingrowing toe nail. A moderate degree of inflammation was associated in the remainder of the toe and contiguous area of the dorsum of the foot. No arterial pulsations were present below the common femoral but the foot showed only slight evidence of ischæmic trophic changes. The right leg showed no pulses below the popliteal. Generalized arteriosclerosis was found on physical examination and considerable calcification of the lower end of the aorta and iliac vessels was found on x-ray. The electrocardiogram showed no gross cardiac abnormality and oscillometric readings confirmed the clinical finding of main artery occlusion.

The patient was treated by bed rest, a protective dry dressing to the toe, correction of his diabetes, and antibiotics. Active exercises of the leg muscles were supervised. After three weeks the gangrene had ceased to progress, involving approximately half of the big toe, the associated inflammation had subsided and skin temperature readings after lumbar sympathetic block revealed a rise of 2° C. on the dorsum of the foot. Histamine flare test resulted in a flare of one inch in diameter on the dorsum of the foot contiguous to the big toe. Surgical therapy of lumbar sympathectomy with amputation of the big toe and first metatarsal head was carried out leaving the wound partially open because of the residual inflammation. Healing was solid in four weeks and the patient returned to his job in six weeks as a mechanic, walking with a slight limp.

CASE 2

J.S., aged 43, was admitted with severe pain in the right foot and a gangrenous ulceration of the little toe. This had followed a blister on this toe subsequent to walking in a new pair of shoes. The right foot and, to a lesser extent, the left showed severe ischæmic trophic changes and both legs had no pulsation in the main vessels below the popliteals. The oscillometric readings in the calves were: right 0.5, left 2.5. At the ankle the readings were 0 and 0.5. The histamine flare test showed practically no response on the right dorsum and less than one inch in diameter on the left but excellent responses in flare production were present in both below knee areas. Right lumbar sympathetic block showed no rise in skin temperature of the foot.

Conservative therapy with bed rest, whiskey ounces two every four hours, cessation of smoking and priscoline, 25 mgm. every four hours continued for two weeks resulted in little improvement. Below knee amputation two and a half weeks after admission resulted in healing by primary intention and the patient returned to his job of sleeping car conductor seven months following his amputation. The clinical diagnosis confirmed by section of the arteries of the amputated specimen was Buerger's disease.

CASE 3

H.K., aged 67, was admitted with small painful areas of gangrene between the third and fourth toes of the left foot. He had a lower third of thigh amputation elsewhere two years previously because of gangrene of the right big toe. He had been treated at home for six weeks prior to the present admission without improvement. Examination revealed relatively severe trophic changes in the toes of the left foot but these changes were not too severe in the foot itself. A kissing area of gangrene was present as above mentioned. Moderate ischæmia on elevation and rubor on dependency was present and no pulse was palpable below the common femoral. The blood sugars were normal and generalized arteriosclerosis was present but without marked cardiac involvement. The response to the histamine flare test was about one-half inch in diameter on the dorsum of the foot and skin temperature increase following lumbar sympathetic block was a dubious half degree C. A transmetatarsal amputation was indicated because of the loss of the right leg but the preoperative tests were dubious in regard to possible healing.

A lumbar sympathectomy and coincident transmetatarsal amputation was carried out one week after admission. Healing of the foot took place but was slow and the patient was in hospital more than a month following operation. He returned to work six weeks after discharge but had only been working three weeks when the scar broke down, pain reappeared and he was readmitted for a supracondylar removal of the remaining leg.

When preoperative evaluation indicates that only a major amputation will result in successful healing of the involved leg many factors enter into the decision whether to carry out the amputation or persist in conservative therapy. There are many cases where a gangrenous toe has finally demarcated and healed after many months of bed rest, but I have found that such a person usually soon develops a new gangrenous lesion after being active again and the whole process is repeated once more. The patient, of course, may settle the problem by re-

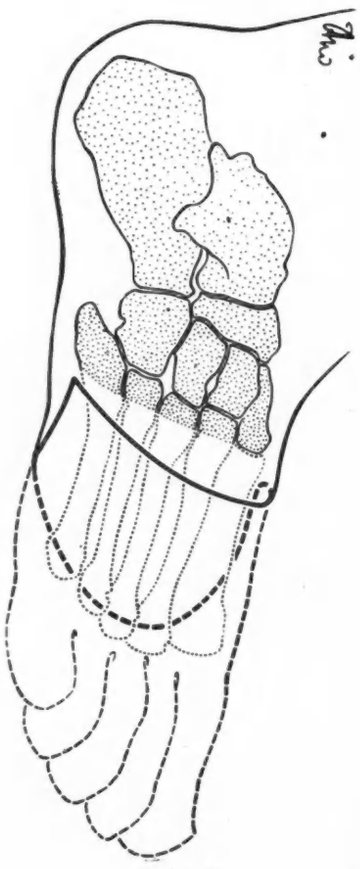

Fig. 4

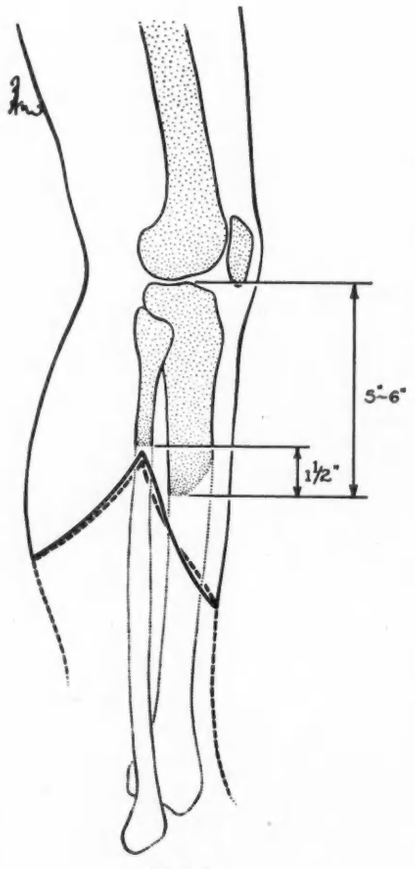

Fig. 5

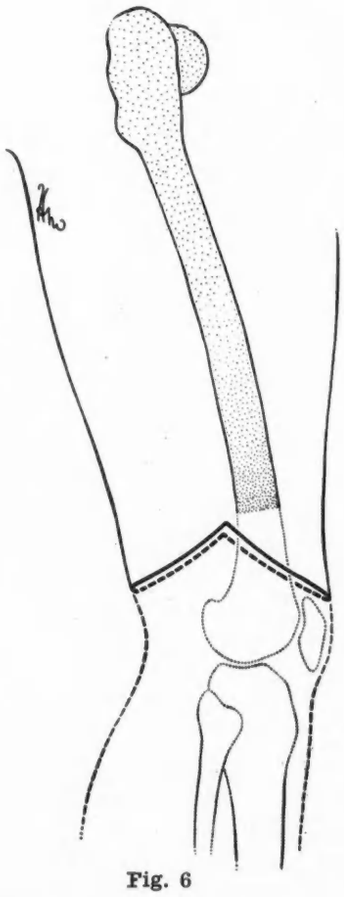

Fig. 6

Fig. 4.—Transmetatarsal amputation. Note that the lateral four metatarsals are sectioned in a straight line from the level of the first tarso-metatarsal joint leaving the bases of these lateral four. **Fig. 5.**—Classical site of election amputation using eqaul flaps, a point which is most important in all amputations for ischæmic arterial disease. disease. **Fig. 6.**—Supracondylar amputation which is unfortunately necessary in the majority of cases of distal gangrene.

fusing amputation but it is my opinion that prolonged conservative treatment is not worth the price from all aspects including financial, hospital bed space and nursing care. Prolonged bed rest leads to a poor morale, weak musculature and, in many, a yielding to the state of chronic invalidism.

Many of these individuals can be rapidly rehabilitated and become active individuals on their artificial limb if salvage is not too long delayed. Judgment must be exercised in the elderly amputee in respect to advising a prosthesis. Well wishing friends or social agencies should be restrained in buying an artificial leg in the case of an individual who shows inability to get about on crutches, especially if the opposite leg also shows severe ischæmic damage. The patient must be assessed for mental alertness, physical ability and morale before the limb is ordered.

TYPES OF AMPUTATION FOR ISCHÆMIC DISEASE

Apart from toe amputations, I believe there are only three other suitable sites for amputation necessitated by arterial occlusive disease. These are the transmetatarsal (Fig. 4), site of election (Fig. 5) and supracondylar (Fig. 6). In all these types, flaps should be equal in length and contain the deep fascia. In the below knee and supracondylar types, the muscle should be divided at the level of bone section and the proximal periosteal stripping should not be more than a half-inch from the cut level of the bone. The Stokes-Gritti and Callander types are ruled out because of the need for a long anterior flap. Absolute atraumatic technique is essential in all such amputations, with the removal of all tags of devitalized tissue produced by the operation. A tourniquet should be used in the supracondylar and below knee operations and blood should be given at time of operation in all elderly individuals.

TABLE I.

MAJOR AMPUTATIONS FOR ISCHÆMIC DISEASE
1946 - 1950

Transmetatarsal	5
Transmetatarsal with lumbar sympathectomy	6
Site of election	12
Site of election with sympathectomy	3
Supracondylar	43
Double amputation thigh	4
Re-amputation thigh:	
Painful stump	1
Infected stump	2
Failure transmetatarsal	4

Table I indicates the major amputations personnally performed at the Royal Victoria Hospital in the past five years. There was no hospital mortality.

SUMMARY

1. With the increasing longevity of the general population there is a gradual increase in the number of leg amputations necessary for ischæmic arterial disease. A marked improvement in the mortality statistics from these amputations has taken place due to improved preoperative assessment, operative technique, and postoperative care. This is well shown in the series presented.

2. The level of probable successful amputation can be determined correctly in most instances by a careful clinical examination and the performance of a definite investigative program. The aim is to save as much functioning limb as possible in these people so as to speed up their rehabilitation and improve their future usefulness.

3. The important points in the clinical examination are discussed and an outline is given of the methods of investigation carried out at the Royal Victoria Hospital. Illustrative case records are presented.

4. A brief discussion of the types of amputation indicated for ischæmic arterial disease is presented.

RÉSUMÉ

Au fur et à mesure que la longévité de la population en général s'accroît, on note une augmentation correspondante du nombre des amputations nécessitées par les troubles d'ischémie artérielle. La mortalité consécutive ces amputations est grandement diminuée, et ce fait tient à ce qu'avant d'intervenir on fait un meilleur bilan de son malade tant du point de vue local que général, que la technique opératoire est améliorée et les soins postopératoires meilleurs.

Dans la plupart des cas on peut déterminer correctement le niveau idéal d'une amputation pour avoir les plus grandes chances de réussite, il suffit de faire un examen clinique très approfondi et s'astreindre à un programme d'enquête locale très fouillée. Le traitement doit être avant tout conservateur, faciliter la réhabilitation des malades aussi vite que possible afin d'en faire des sujets utiles et non des êtres condamnés à la chaise roulante à perpétuété.

D'autre part il peut y avoir des inconvénients à retarder l'intervention majeure quand elle s'impose ou d'amputer d'une façon trop conservatrice. Pour ne pas parler de l'aspect financier de la question, de longue hospitalisation et de soins post-opératoires qui s'éternisent, il n'y a aucun doute que le séjour prolongé au lit a tendance à donner un mauvais moral, une musculature affaiblie et un penchant à l'invalidité sans retour.

DIAGNOSIS AND TREATMENT OF RECENT AND NEGLECTED NASAL FRACTURES*

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Calgary, Alta.

FRACTURES of the nose are probably the most common fractures encountered in practice. The exposed position of the nose makes it vulnerable to injury more than any other part of the face. Yet this type of fracture is more often missed and poorly treated than any other fracture of the body, resulting in ill effects both functionally and cosmetically.

How many men routinely examine an infant's nose shortly after birth? Everyone checks the foreskin of the penis, but very few inspect and palpate the infant's nose for septal deflection, nasal dislocation or fracture. The child travels through a pelvic tunnel undergoing varied contortions and compressions, with the soft nose pressed flat against the face, the septum taking the brunt of the force, often dislocating it. It is a simple procedure to shove the nasal septum manually into the mid line by grasping the tip of the nose with the thumb and index finger often feeling or hearing an audible click on reduction. No instrumentation is necessary. Many practitioners noticing difficulty in breathing will often do a roentgenogram of thymus, when in reality all they have to do is lift up the tip of the nose, and notice the caudal end of the septum pushed out of the columella bed.

ANATOMY OF THE NOSE

The upper 1/3 or bony arch is composed of the thin nasal bones ventrally, and the thick frontal processes of the maxilla dorsally. Fractures usually take place at the junction of these 2 bones.

The lower 2/3 or cartilaginous arch is composed of the upper (triangular) cartilages and lower (alar) cartilages. The upper lateral cartilages are responsible for the shape of the middle one-third of the nose. The ventral borders of the upper lateral cartilages are continuous with the septum and form the wings of the nasal septum. They are regarded as one piece, any deformity of the septum will affect the upper lateral cartilages. The lower lateral cartilages are horseshoe shaped, consisting of a mesial and lateral crus. The mesial crus lies in the columella (mobile portion) the lateral crus extends halfway down the lobule. The angle forms the dome, and is responsible for the shape of the tip of the nose. The lower lateral cartilage overrides the caudal end of the upper lateral cartilage, and acts as a fluttering valve (stopcock) thus controlling the amount and pressure of the air in the nose. Any interference with mobility of this joint will affect the physiology of the nose.

The nasal septum is the key-stone or the buttress of the nose. It is composed of the thin perpendicular plate of the ethmoid, the strong bony portion—the vomer—and the mobile quadrilateral cartilage. The septum at birth is completely cartilaginous with the exception of the vomer. The perpendicular plate begins to ossify during the first year. Trauma to the septum causes it to grow to one side. The mucous membrane of the nose is closely adherent to the bone and cartilage, and as a result most fractures are compounded internally.

PHYSIOLOGY OF THE NOSE

The function of the nose is to warm, humidify and filter the air. The turbinates which are composed of cavernous erectile tissue, break the current up and act as thermostats. A mouth breather neither warms nor humidifies the air, resulting in sore throats, with recurrent upper and lower respiratory infection. The olfactory and phonatory function of the nose are obviously affected by nasal obstruction and will not further be discussed here. The check valve of the lateral cartilages control the volume, pressure and distribution of the inspired air.

Volume.—Too large nares will admit too much air, and too narrow nares cut down the volume.

Pressure.—The nares are smaller than the choanæ. On inspiration there is a negative pressure, on expiration there is a positive pressure. The venous return to the heart is controlled by the negative pressure in the chest. Thus the size of the nares which control the negative pressure in the nose, plays an important part in the circulation of the body. A mouth breather has a poor negative pressure, resulting in shallow breathing and poor circulation. Anterior nasal obstruction causing increased negative pressure, tends to cause collapse of the Eustachian orifices, resulting in impaired hearing.

Distribution of air currents.—According to Bernoulli's principle, negative pressure causes air to rise. On inspiration the air rises, and travels along the middle turbinate. On expiration the pressure is positive, and the air current travels along the floor of the nose. It is for this reason that a person cannot smell his own breath. Nasal obstruction, dependent or unduly elevated nasal tips will cause eddies of air, and drying of the mucous membrane of the nose. This can easily be demonstrated by asking a patient with a drooping nose to place one of the fingers at the nasal tip, and elevate the tip upwards—the patient breathes much more easily.

DIAGNOSIS

Diagnosis is made difficult by the swelling which obscures the fracture and tenderness which prevents palpation, and the roentgenogram cannot always be relied upon. The most reliable method of diagnosis is a good history, the symptoms, and examination of the nose carefully both externally and internally. Always check for a history of trauma—the injury, especially in children may be slight. The direction of the blow helps to determine the displacement.

Symptoms and signs.—These will be discussed in order of frequency. *Epistaxis* is almost a constant sign, since the majority of the fractures are compounded internally, tearing the mucous membrane. The bleeding may be only a few drops of blood, or it may be severe if one of the main arteries are involved. In a greenstick fracture with no tear in the mucous membrane, there is no history of epistaxis, making the diagnosis difficult.

* Read before the Edmonton Academy of Medicine, April 4, 1951.

Swelling is the next commonest sign, but the diagnosis should be made before the swelling appears, as this obscures the true extent of the injury, making the diagnosis more difficult, and often being mistaken for a soft tissue swelling.

Ecchymosis is due to extravasation of blood in the subcutaneous tissue appearing between 7 to 24 hours after the fracture. A black eye is usually thought to be due to a blow on the eye. The eye is well protected by the orbit. Often it is due to a fractured nose, resulting in extravasation of blood in the looser subcutaneous tissue of the eyelids. Always examine the nose in ecchymosis of the eyelids.

Tenderness over the site of the fracture is the next frequent sign. Pain itself is usually absent since there are no muscles in the nose that will pull on the fragments. They are vestigial muscles.

Fractured or dislocated septum is practically always present when there is a fracture. This may be missed because of œdema around the septum. Use vasoconstrictors in a mild anæsthetic base, and examine the septum with an applicator. You can differentiate a recent fracture from an old spur in that there is bogginess, tenderness, mobility and crepitus in a recent fracture. In an old deviation there is scarring, no tenderness and it is not moveable.

Roentgenograms are only positive in a little over 50% of the cases. A positive film makes the diagnosis conclusive, but a negative film by no means rules out the possibility of a nasal fracture, but must be taken for medico-legal reasons. The reasons why the films may be negative is that the nasal framework in children is largely cartilaginous, or only partially ossified. Detail is often lost because in conventional films the nose is too far from the casette. The overlapping skull interferes with the picture. A dental film with a short exposure taken in lateral and Waters position gives the best results.

Obvious bony or cartilaginous deformity is more easily recognized in the absence of swelling. If present it is conclusive. The same with *crepitus*, but the latter is present in only about 15% of the cases.

Nasal obstruction may be due to a fractured or dislocated septum, œdema of mucous membrane, or a submucous hæmorrhage. If hæmatoma is present, incise the mucous membrane at once, aspirate or curette the clot and pack, otherwise it will result in either an abcess, perforation, or absorption of the clot with subsequent fibrosis, and nasal deformity. Hæmatoma of the upper or lower lateral cartilages result in perichondritis, fibrosis and curling of the cartilages similar to a cauliflower ear.

Periorbital emphysema is due to air in the subcutaneous tissue following a tear in the mucous membrane. The patient should be warned against blowing the nose following a fracture. It is not frequently present.

Thus in a child even with a history of minor trauma, followed by slight epistaxis and tenderness, treat as a nasal fracture even if the roentgenogram is negative.

TREATMENT

The most important part in the treatment is the proper diagnosis. Needless to say, the shock and control of the hæmorrhage are the primary considerations. Examine for fractures elsewhere. If there is escape of cerebrospinal fluid do not reduce the fracture, as the cribriform plate is involved. Wait at least ten days and use chemotherapy and antibiotics to prevent meningitis. If the nasal pyramid is driven into the skull, do not reduce, wait six months, and then do a rhinoplasty.

If there is soft tissue injury, convert the compound into a simple fracture if seen within eight hours. Clean the wound well, otherwise carbon particles may cause tattooing. Only conservative debridement should be done, as any injudicial sacrifice of skin will impair the cosmetic result. Since the blood supply of the face is extremely good, isolated pieces of bone and cartilage should be replaced, as it is rare for sequestration to occur in the nose. If there is a large wound and it can not be approximated, skin graft at once from the upper eyelid or the post-auricular area. If seen after eight hours, suturing is delayed until infection is controlled.

Bony and cartilaginous reduction.—The nasal bones, upper and lower lateral cartilages, and the septum must be replaced. In children general anæsthesia has to be used with post-nasal plugs. Intratracheal anæsthesia through the mouth is good. In adults local anæsthesia is very satisfactory, but if intravenous anæsthesia is used post-nasal plugs must be inserted.

Linear fractures are simple fractures without

displacement or comminution. No reduction is necessary.

Greenstick fracture is the hardest to diagnose since there is no epistaxis. After the swelling subsides, a mild curvature of the nose is noticed. This is the type that is usually seen in children. The only way to diagnose this type is to do an exploratory reduction. The fracture is usually at the junction of the nasal bones with the maxilla. Complete the fracture by application of force in the reverse direction of the fracture, then mould into position. The septum is rocked between Walsham or Ash forceps and elevated into position on the vomer.

Lateral fracture.—This is due to a blow from the side and is the commonest fracture encountered. The displacement is at the junction of the nasal bones and the frontal process of the maxilla. The concave side is the side of impact, convex on the opposite side. The nasal septum is usually fractured at the junction of the quadrilateral cartilage and vomer, with the deviation to the opposite side of impact. If there is no overriding, no instrumentation is necessary for reduction. With the thumb placed on the convexity, a vigorous thrust will restore the nose in mid position. An audible click results. If overriding is present, the depressed nasal bones must be unlocked before you can elevate them. With forceps, the nasal process of the maxilla on the concave side must be fractured outwards, and then the nasal bones are elevated with a blunt instrument or forceps, and moulded into place by external manipulation. The septum is placed in mid line with either Walsham or Ash forceps. If there is overriding of the septum, and it cannot be replaced, elevate the muco perichondrium and pry the cartilage fragments into place. If there is buckling, and the cartilage springs back, remove the cartilage, and replace with a straight piece of preserved septal cartilage.

Fracture from an anterior blow results in a depressed nasal fracture with a saddle deformity. The nasal bones are depressed and are locked under the nasal process of the maxillæ, and must be fractured outward in order to unlock the nasal bones. Then elevate the nasal bones ventrally with a blunt instrument intranasally or use a forceps with a blade on each side of the septum. The septum is restored in mid line as outlined in lateral deviation. Since the septum is badly comminuted, a batten of cartilage should be placed subcutaneously on the dorsum of the nose. The upper lateral cartilages which were depressed usually elevate automatically when the septum is elevated.

Fracture from below (caudal blow) causes the nasal bones to be driven superficial or deep to the nasal process of the frontal bones. If superficial, the naso-frontal angle will be lost. If deep, the naso-frontal angle will be increased. The septum breaks off from the anterior nasal spine. Reduce the nasal bones by pulling the fragments caudally with forceps and manipulate into place by external pressure. Replace the septum as outlined previously.

Stabilization of fragments.—There is no displacement as a rule after reduction, as there is no pull of the fragments by the muscles. The periosteum and perichondrium will act as splints. Intranasal packing is the only splinting required, not only to hold the fragments in place, but to prevent hæmatoma. With the use of antibiotics and chemotherapy, packing may be left in place 4 to 6 days. In greenstick fractures there is no need to use any packing. There is no need to use intranasal or external splints in any fracture. If intranasal packing will not hold the fragments in place, nothing else will, and the patient is warned that a rhinoplastic procedure will have to be done at a later date. External splints and through and through sutures over buttons cause skin necrosis due to subsequent swelling. Dental stent, after application of adhesive tape and felt should be used. It is used more for protection than actual splinting of the fragments.

NEGLECTED FRACTURES

The ideal time to reduce a nasal fracture is within the first 24 hours before swelling sets in. After that it is best to wait 5 to 7 days for the swelling to subside. The fracture should be reduced before 2 weeks, the latest 3 weeks, after that the bones are fixed and reconstructive surgery is necessary. Poor nasal function and nasal deformities in adults are very often due to neglected fractures in childhood. The deformity often does not show up until years later, when the nose and face undergoes development.

To properly treat these nasal deformities, the nose must be carefully analyzed. You must consider the three components of the nose—whether it is due to the bony portion, the lateral cartilages or the septum. The nose must be reconstructed both internally and externally. What good would it do to do a submucous resection,

if the obstruction is due to deviated nasal bones, or hypertrophied or collapsed lateral cartilages?

Bony portion.—Any lateral deviations must be refractured and replaced in the mid line. If there is a hump and a lateral deviation, a larger piece is removed from the concave side during the removal of the hump. Anterior blows resulting in saddle noses are often not noticed until the child matures. Cartilage is replaced by fibrous tissue, causing an indrawing in the middle 1/3 of the nose. In reconstruction of a saddle nose a graft must be used. Cancellous bone from the hip is best as it is easily moulded and is resistant to infection. Rib cartilage tends to curl. A greenstick fracture at the bridge of the nose with excessive callus formation results in a humped nose. This does not show up until adolescence. The treatment here is to remove the hump and narrow the nose.

Cartilages.—It is not sufficient to operate on the bony portion of the nose, and ignore the cartilaginous portion as this would result in a disproportioned nose. It is also important functionally to reconstruct the cartilages as pointed out in the section of physiology.

Septum.—People will often do nothing about their noses because they heard of a friend who had a submucous resection without any benefit. No benefit will be obtained unless all the deviations of the septum are removed. We have always been taught that the septum acts as a buttress of the nose, and in doing a submucous resection the ventral and caudal ends of the septum must be left intact, otherwise a saddle nose will result. If only the posterior (bony) part of the septum is deviated, then the regular Killian operation will suffice. If however, the ventral or caudal ends of the septum are deviated then these must be removed and replaced with straight cartilage or rhinoplastic procedures carried out removing the ventral and caudal portions of the septum.

SUMMARY AND CONCLUSIONS

1. Examination of the newborn for dislocation of the nasal septum should be routine, and reduction carried out immediately.
2. Nasal obstruction and deformities affect the physiology of the nose and indirectly affect the throat, lower respiratory tract, and circulation of the body.
3. In children, a history of nasal trauma followed by epistaxis and tenderness must be treated as a fracture in spite of a negative roentgenogram. A diagnostic reduction should be carried out.
4. In recent fractures all components of the nose must be properly reduced.
5. Neglected fractures must be treated from a functional as well as cosmetic point of view.
6. It is not sufficient to do only a submucous resection in mechanical nasal obstruction. The whole nose must be taken into consideration.

REFERENCES

1. PROETZ, A. W.: Applied Physiology of the Nose, Annals Publishing Co., St. Louis, 1941.
2. FOMON, S. *et al.*: *Arch. Otolaryng.*, **39**: 608, 1948.
3. BECKER, O. J.: *Arch. Otolaryng.*, **48**: 344, 1948.
4. FOMON, S.: *Ann. Surg.*, **54**: 107, 1936.
5. ERSNER, M. S.: *Penn. Med. J.*, May, 1946.

EFFECTIVENESS OF MODERN TREATMENT FOR GONORRHŒA IN WOMEN

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REINFECTION or treatment failure? This has been a constant question in the minds of those physicians who are treating gonorrhœal infections which do not apparently respond to a single injection of penicillin. There is little assistance to be gained by listening to the protestations of innocence on the part of the venereally infected patient, for the old adage that "All men are liars" is particularly applicable to these cases.

Figures have been published from time to time by various clinicians and from various centres, giving the percentage cure rate for gonorrhœa, or alternately, the percentage failure rate, with various schedules of treatment. This "failure rate" appears to have varied between 4 and 6% in different centres.

In contrast to this, Lloyd Jones and Maitland published their figures in England in 1945,[1] which gave a cure rate of over 99.6%. Their cases were all male naval personnel who were admitted and detained in hospital for a period of seven days. They were treated with 150,000 units of aqueous penicillin, two-hourly, over a

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period of eight hours. The amount of penicillin used was considerably less than the amount generally used today in this country, but on the other hand, their patients—though not kept in bed—were prevented from acquiring reinfection.

With this report in mind, it was decided to carry out a similar investigation on *female* patients treated at the Venereal Disease Clinic at a local gaol centre in Vancouver, B.C. This study was further prompted by the fact that in no instance could a case be recalled where a single course of treatment had not effected a cure at this institution.

The patients selected for this study were only those who were found at their initial examination to have a positive smear or culture, or both. Furthermore, they were all patients who were held long enough to be subjected to three successive tests of cure at weekly intervals.

For this study, 100 consecutive cases were reviewed, and in all instances they were found to be clinically and bacteriologically negative on each successive test of cure. The cure rate was therefore 100%.

The amount and type of treatment varied to some extent, as shown by the following table:

TABLE I.

No. of cases treated	*Type of treatment*	*Amount*	*Method*
31	Penicillin (aqueous)	200,000 U.	2 x 100,000 U. at 4 hour interval
61	Penicillin (depo type)	1,200,000 U.	Single injection
3	Penicillin (depo type)	2,400,000 U.	4 daily injections (for complicating salpingitis)
*1	Penicillin (aqueous)	5,760,000 U.	*See note.
4	Streptomycin	0.5—1.0 gm.	2 single injections 2 x 2 injections

*The one case which was treated with 5,760,000 units of penicillin had also a syphilitic infection.

It will be observed that these patients were treated on a variety of schedules, but in all instances their subsequent three tests of cure were negative and no case required retreatment.

The number of cases in this study was comparatively small, and the results are perhaps on that account statistically of limited significance.

However, it does tend to confirm the view that gonorrhœal infections will respond to most of the penicillin treatment schedules at present employed, and that retreatment should rarely be necessary. This study further tends to support the view that most of those cases requiring retreatment are, in fact, the subjects of reinfection, in spite of their protestations of innocence.

As a corollary to this study, it was of interest to note that 55 of these patients had previously been treated for syphilis, thus indicating the high venereal disease rate among those women who ultimately serve gaol sentences.

Blood tests were carried out at four and six months following their treatment in gaol. In no instance did any person who had a negative blood at the time of treatment, subsequently develop a positive Kahn test during the six months' period.

Moreover, in no instance did any patient who had a positive blood test at the time of treatment, subsequently develop a rise in the Kahn titre. This was probably largely a matter of "good fortune" in many instances, and particularly in those treated with 200,000 units of penicillin and with streptomycin.

There is much evidence now to show, however, that quantities of penicillin exceeding one million units are sufficient to abort almost all cases of incubating syphilis and to cure a fairly high percentage of early fully developed infections.

It was with this end in view that the practice was adopted in this province of treating all gonorrhœa infections with a single injection of 1.2 million units of procaine penicillin in oil, with 2% aluminum monostearate.

This may have accounted for the complete absence in this series of any instance of syphilitic infection appearing in the six months' period subsequent to treatment for gonorrhœa.

REFERENCE

1. LLOYD JONES, T. R., MAITLAND, F. G. AND ALLEN, S. J.: Penicillin in Gonorrhœa, *Lancet*, 1945.

POSTGRADUATE COURSE (October 25 and 26, 1951).—Postgraduate Course at Sunnybrook Hospital, Toronto. Subjects of particular interest to general practitioners given by the staff of the University of Toronto. Sponsored by the University of Toronto Medical Alumni Association.

ADRENAL INSUFFICIENCY IN CHILDHOOD*

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THE classical signs of adrenal insufficiency were first described by Thomas Addison in 1855.[1] The chief clinical features of this disease are asthenia, vomiting, hypotension, brown pigmentation of the skin and mucosa and disturbances in the carbohydrate, protein and mineral metabolism. The fasting blood sugar level is usually depressed and an abnormal sensitivity to insulin is frequently encountered. The biochemical findings usually reveal a diminished serum sodium (normal 137 to 146 meq./1); a diminished serum chloride (normal 95 to 108 meq./1); and an increased serum potassium (normal 4.6 to 5.6 meq./1). In addition to the above there is a marked increase in urinary chloride excretion and the 17-ketosteroid excretion in the urine may be markedly diminished. Excess loss of salt and water by the kidneys may lead to dehydration with a consequent rise in the non-protein nitrogen. Post-mortem examination frequently reveals hyperplasia of the lymphoid tissue of the body including the thymus. There may be marked reduction in the size of the viscera, most notably the heart. The adrenal glands in all cases have either been destroyed by some infection such as tuberculosis, or have undergone a complete but unexplained atrophy. This picture is one of complete or pan-hypoadrenalism.

The main features of adrenal cortical insufficiency have been recognized by the medical profession for years. It is only more recently, however, as a result of the studies of Albright,[2] Kendall,[30] Selye,[3] Thorn,[4] etc., that the various functions of the adrenal cortex have been brought to light. Altogether a score or more of different chemical substances have been isolated from the adrenal cortical tissue. Practically speaking the effects of all these various substances may be grouped under one of the following three headings: (a) regulation of the electrolyte balance of the body; (b) regulatory action on the carbohydrate and protein metabolism; (c) influence on secondary sex characteristics coupled with changes in nitrogen metabolism.

A glance at the chemical formulæ of a few of these substances is helpful in understanding their activity and the nomenclature commonly used in the literature. The cyclopentenoperhydrophenanthrene nucleus is common to all these substances. In general, it has been found that steroids which are lacking in an oxygen atom at the C11 position, hence the name "desoxy", are most effective in regulating the mineral balance, especially the retention of sodium and the excretion of potassium. These compounds are frequently referred to as "mineralocorticoids". Compounds, such as corticosterone and 11-dehydro 17 hydroxycorticosterone (cortisone) which have an oxygen atom at C11, produce their main effects on carbohydrate metabolism and are referred to as "glucocorticoids". They aid in the breakdown of protein to amino acids and thereby facilitate their conversion to glucose. They may also have an accelerating effect on the rate of gluconeogenesis by the liver, and, by interference with the action of insulin they tend to raise the level of the blood sugar. An increase in these 11-oxysteroids also brings about a reduction in the lymphoid tissue in the body and a fall in the circulating eosinophiles. The third group of substances, the androgens or "androgenic corticoids" are not so readily labelled. Some are excreted in the urine as 17-ketosteroids. It is believed that in the female practically all, and in the male about two-thirds of the urinary 17-ketosteroids originate in the adrenal cortex. The normal 24 hour excretion of these substances under 7 years is 0.65 mgm. or less,[5] and it rises to 4 mgm. at 7 to 12 years and 8.2 mgm. at 15 to 17 years.[6] These androgenic substances have a marked nitrogen storing effect as well as an influence upon secondary sexual characteristics, such as facial and pubic hair and an increase in size of external genitals.

With the discovery that separate effects were produced by these various adrenal cortical substances, a number of types of adrenal "insufficiency" have come to light, many of which do not show the full picture of Addison's disease. Complete destruction of adrenal function is very rare in childhood and has until

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recently been an extremely acute and fatal affair. A severe septicæmia, such as is seen occasionally in infections with meningococcus may cause hypofunction of the adrenal glands, leading to hyperpyrexia, vomiting, dehydration and circulatory collapse. This is the so-called Waterhouse-Friderichsen syndrome. It is not our intention to deal further with this condition in this paper, but to refer to the somewhat less acute and subacute types of adrenal hypofunction first described by Wilkins, Fleishmann, Howard;[10] Butler, Ross and Talbot;[8a, b] Thelander and Cholffin.[9a, b].

Male infants may also show some increase in genital size, but being isosexual in character these are less conspicuous. Both sexes may also show a marked increase in 17-ketosteroid excretion in the urine. In those cases where serum electrolytes were estimated the sodium and chloride values were usually reduced, while those for potassium were increased.[12, 13, 14] It is unusual, however, to find significant lowering in the blood sugar. Pigmentation has been seen only rarely. In some cases which have survived as a result of treatment, pigmentation has become evident later.[8a, b, 11, 12, 13a, b]

TABLE I.*

Number	Onset	Death	Sex	Gastrointestinal disturbance	Dehydration	Growth disturbance	Weakness	Cardiovascular collapse	Infection	Pigment	Virilism	Family history	Na	Cl	K	NPN	FBS	CO_2	Na	Cl	K	17-KS	External genitals	Internal genitals	Adrenals
8	2W	A	M		+	+	+	+	+	+	+	?	124	103	10	68	N		69	60		65	M		
9	B	6Y	M	+	+	+		+	+		+	+					74						M	M	74g.
10	?	3Y	M					+			+												M	M	
11	11D	A	M	+	+		+	+	+	?	+		121	108	11			15	inc.	inc.		2.5	M		
12a	9D	4M	F	+	+	+	+	+	+		+		135	110		89	61						P	F	14g. PF
b	1M	?	F	+	+		+	+	+		+	+	137	92		43	65	17					P	F	17g.
c	B	7M	F	+		+		+	+	+	+	+		102									P	F	11g.
d	B	8W	M	+	+	+	+	+	+								69						M		21g.
13	B	A	M	+	+	+		+	+	+	+		130		7.9		36	20				5.7	M		
14	18D	5M	M	+	+		+			+			132		6			20					M		
HSC	1W	A	F	+	+	+		+	+	+	+		120	100	7.4	58	102					8.6	P	F	
HSC	B	43D	F	+	+	+	+	+	+	?	+		116	97	12.2	40	159						P	F	19g.

* Other cases since reported and not included in chart—T. C. Panos, *Pediatrics*, **6**: 972, 1950. M. M. Mazursky and E. Swan, *J. Pediat.*, **36**: 789, 1950.

Legend:
A—alive
Y—years.
W—weeks.
M—months.
D—days.
B—birth.
P—pseudo-hermaphrodite.
HSC—present cases.
Number in column I refers to Bibliography.

From a review of the literature it is seen that the most striking feature, in the majority of cases, is the onset of symptoms within a few days or weeks of birth. Vomiting and diarrhœa are frequently seen in the absence of any infection, and in not a few cases these have led to the erroneous diagnosis of pyloric stenosis or intestinal obstruction.[9, 11, 16] Another characteristic finding is the marked difficulty in hydrating these infants either by mouth or with large amounts of parenteral fluid therapy. In female infants pseudohermaphroditic changes, *i.e.*, enlargement of the clitoris and labia majora, hypoplasia of the uterus, occasionally associated with other genitourinary abnormalities, are frequently encountered.

Post-mortem examination of these infants has been most enlightening. Instead of a small atrophic gland one usually finds an organ which may be 5 to 10 times its normal size (Fig. 2). In some cases it has been noted to be as large as the kidney itself. The surface of the gland is markedly convoluted and resembles cerebral cortex. Microscopically the hypertrophy and hyperplasia of the cortex is confirmed and the medulla appears normal. Many authors have tried by the use of a special staining techniques, *e.g.*, Ponceau-Fuchsin, etc., to demonstrate the persistence of the fetal or androgenic zone and the presence of fuchsino-

phil granules with varying success.[9, 10, 12, 15, 17] In two of the cases adrenal cell rest tumours were found in the testes.[9a, b, 11] The following case histories will serve to illustrate the clinical picture presented by these infants.

CASE 1

L.K., this infant was first seen at 6 weeks of age for treatment of a hypospadias. Further enquiry revealed that she had vomited after almost every feeding since birth and had failed to regain her birth weight.

On examination she was seen to be poorly developed, poorly nourished, hypotonic and dehydrated. There was a purulent discharge from the right eye. Her liver was palpable 1 cm. below the right costal margin. The only other abnormality concerned the external genitalia. The clitoris was hypertrophied. There was a small slit-like vaginal orifice at the base of the clitoris and the urethral orifice was situated in the anterior wall of this small vagina. The labia majora were large and resembled loose empty scrotal sacs which had not fused. The serum sodium on admission was 120 meq./1; serum Cl 100.4 meq./1; and serum K was 7.4 meq./1. At this time a diagnosis of adrenogenital syndrome complicated by conjunctivitis and dystrophy was made.

In hospital she continued to regurgitate after almost every feeding and occasionally to vomit (Fig. 1). She took her feedings reluctantly and despite parenteral fluid supplement she continued to be clinically dehydrated. She developed diarrhœa and because of continuing refusal of feedings, the appearance of a cough and dehydration she was started on intravenous fluids, 1 gm. oral salt and 5 cc. of adrenal cortical extract (A.C.E.) q. 4 hr. daily. Chest x-rays at this time revealed bronchiolitis with obstructive emphysematous changes, and a small heart shadow. This infection cleared with the use of antibiotics and chemotherapy.

As part of a therapeutic test the A.C.E.* and salt were discontinued, and within a few days she developed fever, diarrhœa, vomiting, began to refuse feedings and became dehydrated. With reinstitution of intensive therapy she improved and the serum electrolytes returned to normal. Except for one further exacerbation of fever, vomiting, diarrhœa and dehydration she continued to do well and was discharged home on a diet containing 2 gm. added salt daily.

* Cortin=Adrenal cortical extract (A.C.E.) Connaught Research Laboratories, 1 c.c. = 30 rat units.

At 6 months of age she was readmitted to hospital because of slow weight gain despite adequate food and fluid intake and poor appetite. She was weak and listless and her skin had become dry and loose.

The significant findings on this admission (Fig. 2) were dystrophy, dehydration, poor postural tone, fever with no obvious source of infection, and a definitely dark cast to her skin, especially over her knees and elbows. Investigation revealed the serum sodium to be 138 meq./1; Cl 103.2 meq./1; K 8.2 meq./1; fasting blood sugar 102 mgm. %; non-protein nitrogen 58 mgm. %; and the 24 hour excretion of 17-ketosteroids in the urine was 8.59 mgm. %. Parenteral fluid therapy was instituted on admission. On her second hospital day 5 c.c. A.C.E. was started twice daily for 3 days and then only once daily for 3 days. On this therapy her hydration improved slowly and she began to gain weight. On her third hospital day 0.5 mgm. desoxycorticosterone* acetate in oil (intramuscularly) and 2 gm. oral salt daily were started and maintained for 3 weeks, until her 20th hospital day when 2 pellets, each 75 mgm. of desoxycorticosterone acetate were implanted subcutaneously in the subscapular region. Her postoperative course was complicated by fever and diarrhœa which cleared with symptomatic treatment. She continued to be well regulated on 2 gm. added salt daily until 15 months of age. At this time, 9 months after the implantation of the pellets, she was readmitted to hospital, because she had become irritable, restless, feverish, and had developed vomiting and diarrhœa.

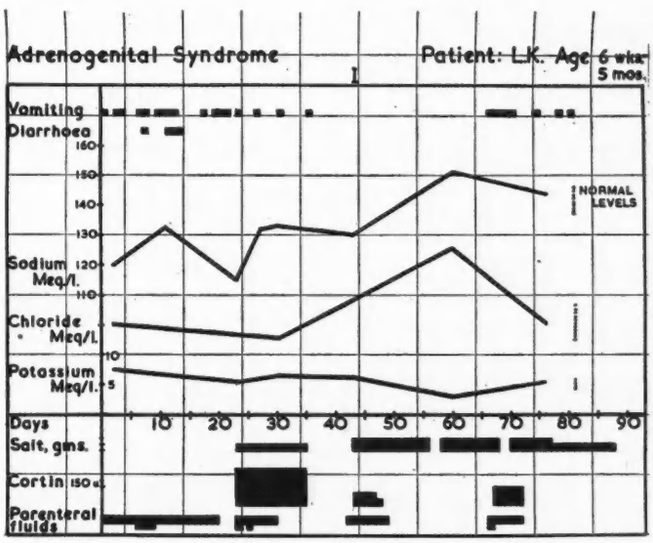

Fig. 1

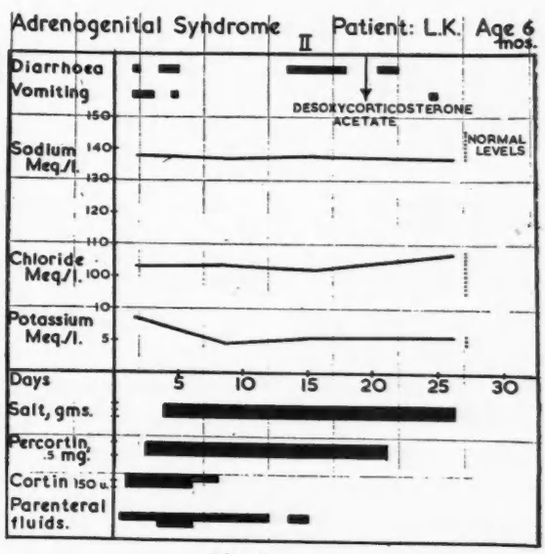

Fig. 2

On examination she was well developed, well nourished and only slightly dehydrated. Both eardrums were injected and her tonsils were moderately enlarged. The external genitalia were the same as on previous admission. Her skin was still deeply tanned, especially over exposed areas, around her knees and elbows. The serum sodium was 115 meq./1; Cl 81 meq./1 and K was 6.0 meq./1 (Fig. 3).

She was given a stat dose of 1 gm. oral salt and 2 gm. daily thereafter for 3 weeks. On her 4th hospital day she was started on 0.5 mgm. percortin, and in 5 days because of continuing dehydration this was increased to 1 mgm. daily. Percortin therapy was discontinued when 2 pellets of DOCA, each 75 mgm. were implanted subcutaneously. Three weeks after admission a laparotomy to determine her true sex was performed and a small, infantile uterus, normal Fallopian tubes and ovaries were found. Biopsy of one ovary revealed normal ovarian stroma containing numerous primordial follicles. The size of her adrenals could not be accurately evaluated

* Percortin=Desoxycorticosterone acetate in oil.

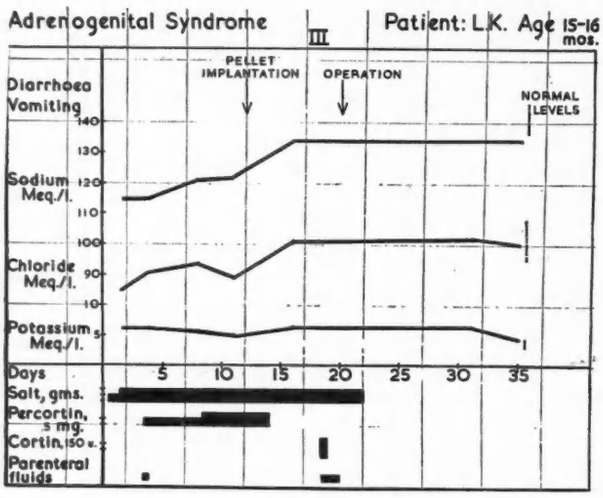

Fig. 3

at this time. An amputation of her clitoris was then performed. On the day of operation she received 450 rat units of cortin as well as her daily dose of percortin. Her postoperative course was relatively uneventful.

Since then she has remained well regulated despite frequent upper respiratory tract infections for which a tonsillectomy and adenoidectomy was performed. She was last seen at 29 months of age, 14 months after the second implantation of DOCA pellets. At this time her serum electrolytes were within normal limits. She appeared well and active but the skin was still quite darkly pigmented.

CASE 2

The second case, M.McI. was similar in nearly all respects to the first case presented. The essential findings are shown in Fig. 4. Unfortunately this child developed an aspiration pneumonia and died.

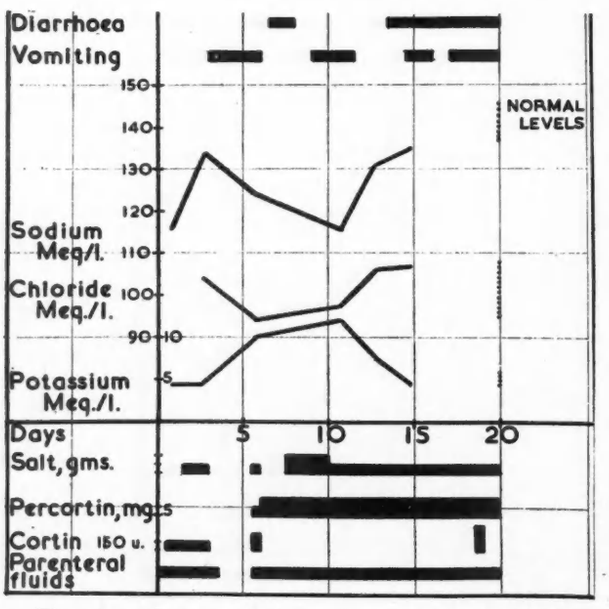

Fig. 4.—Adrenogenital syndrome patient, M.McI., admitted, age 3 weeks, died 6 weeks.

These cases illustrate a type of adrenal insufficiency which is seen in childhood usually within the first few weeks of life. A condition which is misdiagnosed in many cases as being due to some parenteral infection or possibly to intestinal obstruction. They illustrate the complex changes which may occur. Apparently there was a marked deficiency or absence of the "mineralocorticoids" leading to severe dehydration. Though "glucocorticoid" excretion in the urine was not determined, the glucocorticoids may be considered normal since the glucose tolerance tests and the fasting blood sugar levels were within normal limits. The "androgenic corticoids" on the other hand were markedly increased as evidenced by the changes in the secondary sex characteristics, and by the large amount of 17-ketosteroids excreted in the urine. From this discussion it is apparent that the adrenal cortex of a single individual may exhibit hypoactivity of the mineralocorticoids, normal activity of the glucocorticoids and hyperactivity of the androgenic corticoids at one and the same time.

Fortunately, as the result of the work on Addison's disease, a great deal concerning the treatment of the mineralocorticoid deficiency is now known.[2, 4, 20 to 24] If these patients are discovered early, they can probably be carried as in our first case by repeated injections of DOCA in oil or by implantations of desoxycorticosterone acetate pellets. Sufficient time has not elapsed since these cases were first recognized to give the ultimate prognosis. Some of these children later in life may develop some mineralocorticoid hormone production. On the other hand they may, like the Addisonian patient, require replacement therapy for the rest of their lives. Gardner *et al.*[8b] have recently reported the follow-up studies on the case first described by Butler, Ross and Talbot. This boy is now 11 years old and apparently still receives DOCA.

DISCUSSION

It has been suggested that the various layers of the adrenal cortex produce their own specific hormones. To date there is only suggestive evidence to support this thesis. It has further been suggested that a persistence of the fetal or "androgenic" zone into post-natal life might be responsible for the excess production of adrenal androgens. Most investigators have failed to demonstrate this phenomenon.[8, 9, 25 to 28] The possibility that an inherited character, or some upset in the endocrine metabolism of the maternal

organism might influence the development of the fetus is suggested by the frequent occurrence of more than one case in a single family.[8, 9, 12, 15, 16]

This paper has been confined almost entirely to a discussion of insufficiency of mineralocorticoids. On theoretical grounds, it should be possible to postulate that deficiency states might occur involving the glucocorticoids* and also the androgenic corticoids. In regard to the former, we know that there are a number of children who suffer from marked degrees of hypoglycæmia in the early days of life, which may persist for months and lead to mental deterioration. In a number of these cases which have been investigated at our hospital in conjunction with the Department of Banting and Best Medical Research, University of Toronto, no evidence of increased insulin activity could be demonstrated either by insulin assays or in serial sections of portions of tissue removed at sub-total pancreatectomies. While this is not direct proof, it does lend indirect support to the possibility that some of these cases may be due to adrenal insufficiency of the glucocorticoids leading to an overactive response to normal amounts of insulin secreted by the individual's own pancreas. Some cases have been treated with ACTH. McQuarrie[31] reports that this substance produces favourable response only as long as it is administered. The effect of ACTH indicates that some 11-oxysteroid activity is present in the adrenal but does not indicate the possibility of sub-normal activity prior to the administration of ACTH. The very small quantities of 11-oxysteroids present in these infants makes direct determination difficult. Lack of androgen formation by the adrenal cortex is probably of little importance especially in the male, since this function is probably taken over to a large extent by the gonads. It might conceivably be responsible for some of the cases of asthenia and lack of muscular development in apparently otherwise normal children.

SUMMARY

The literature on adrenal insufficiency in childhood has been reviewed. There is a period shortly after birth when a number of children may show marked evidence of adrenal insufficiency particularly with regard to the mineralocorticoids. Their clinical picture may often be confused with intestinal obstruction or pyloric stenosis. At the same time excessive androgen formation by the adrenal frequently leads to abnormalities in the genito-urinary apparatus.

Two cases which were observed at the Hospital for Sick Children have been added to the series. In one case the implantation of pellets of desoxycorticosterone acetate has proved to be life-saving, and this child is apparently well and active 29 months after the initial treatment.

* Since this paper was written a case of glucocorticoid insufficiency has been described in infancy by L. J. Geppert and W. A. Spencer.[32]

REFFRENCES

1. ADDISON, T.: On the Constitutional and Local Effects of Disease of the Suprarenal Capsules, D. Highley, London, 1855.
2. (a) ALBRIGHT, F.: *J. Clin. Endocrinol.*, 1: 375, 1941. (b) *Harvey Lectures*, 38: 123, 1942-43.
3. SELYE, H.: Textbook of Endocrinology, Acta endocrinologica, Univ. de Montreal, Montreal, Que., 1950.
4. THORN, G., FORSHAM, P. H. AND EMERSON, K.: The Diagnosis and Treatment of Adrenal Insufficiency, Chas. C. Thomas, Springfield, Ill.
5. TALBOT, N. B., BUTLER, A. M., BERMAN, R. A., RODRIGUEZ, P. M. AND MACLACHLAN, E. A.: *Am. J. Dis. Child.*, 65: 364, 1943.
6. FRASER, R. W., FORBES, A. P., ALBRIGHT, F., SULKEWITCH, A. AND REIFENSTEIN, E. C. JR.: *J. Clin. Endocrinol.*, 1: 234, 1941.
7. WEINBERG, L. D. AND MCGARRACK, T. H.: *New England J. Med.*, 232: 95, 1945.
8. (a) BUTLER, A. M., ROSS, R. A. AND TALBOT, N. B.: *J. Pediat.*, 15: 831, 1939. (b) GARDNER, L. I., SNIFFEN, R. C., ZYGMUNTOWICZ, A. S. AND TALBOT, N. B.: *Pædiatrics*, 5: 808, 1950.
9. (a) THELANDER, H. E. AND CHOLFFIN, M.: *J. Pediat.*, 18: 779, 1941. (b) *Idem*: *J. Pediat.*, 29: 213, 1946.
10. WILKINS, L., FLEISHMANN, W. AND HOWARD, J. E.: *Endocrinology*, 26: 385, 1940.
11. DARROW, D. C.: *Yale J. Biol. & Med.*, 16: 579, 1943.
12. ZUELZER, W. W. AND BLUM, A.: *J. Pediat.*, 35: 344, 1949.
13. (a) TEPPER, W.: *J. Pediat.*, 34: 768, 1949. (b) BARNETT, H. L. AND MCNAMARA, H.: *J. Clin. Investigation*, 28: 1498, 1949.
14. MOORE, F. P. AND GERMAK, E. G.: *J. Pediat.*, 36: 91, 1950.
15. ALLIBONE, E. C., BAAR, H. S. AND CANT, W. H. P.: *Arch. Dis. Childhood*, 22: 210, 1947.
16. DIJKHUIZEN, R. K. AND BEHR, E.: *Acta Pediat.*, 27: 279, 1940.
17. HARRIS, C.: *Arch. Dis. Childhood*, 21: 178, 1946.
18. SKELTON, M. D.: *Arch. Dis. Childhood*, 20: 135, 1945.
19. EVANS, P. R. AND SHELDON, W.: *Proc. Roy. Soc. Med.*, 30: 1190, 1937.
20. (a) LOEB, R.: *Am. J. Med.*, 7: 100, 1949. (b) *Idem*: *J. A. M. A.*, 116: 2495, 1941. (c) *Idem*: *Bull. New York Acad. Med.*, 18: 263, 1942. (d) *Idem*: *Proc. Soc. Exper. Biol. & Med.*, 30: 808, 1933.
21. THORN, G. W., GARBUTT, H. R., HITCHCOCK, F. H. AND HARTMAN, F.: *Endocrinology*, 21: 202, 1937.
22. FORSHAM, P. H., THORN, G. W., BERGNER, G. E. AND EMERSON, K. JR.: *Am. J. Med.*, 1: 105, 1946.
23. GAUDINO AND LEVITT: *J. Clin. Investigation*, 28: 1487, 1949.
24. HARRISON, H. E. AND DARROW, D. C.: *Am. J. Physiol.*, 125: 631, 1939.
25. BROSTER, L. R. AND VINES, H. W. C.: The Adrenal Cortex—A Surgical and Pathological Study, H. K. Lewis & Co., London, 1933.
26. FUJIWARA, T. F.: *Arch. Path.*, 27: 1030, 1939. *Surg., Gynec. & Obst.*, 74: 281, 1942.
27. (a) CAHILL, G. F., MELICOW, M. M. AND DARBY, H. H.: *Surg., Gyn. & Obst.*, 74: 281, 1942. (b) *New England J. Med.*, 218: 803, 1938.
28. GROLLMAN, A.: The Adrenals, Williams and Wilkins Co., Baltimore, 1936.
29. KRABBE, K. H.: *New York Med.*, 114: 4, 1921.
30. KENDALL, E. C.: *Quart. Biol.*, 5: 299, 1937.
31. MCQUARRIE, J., BAUER, E. G., ZIEGLER, M. R. AND WRIGHT, W. S.: Proceedings of the First Clinical ACTH Conference, 1950. J. R. Mote, M.D., Blakiston and Company, Philadelphia, Pa.
32. GEPPERT, L. J., SPENCER, W. A. AND RICHMOND, A. M.: *J. Pediat.*, 37: July, 1950.

THE SCALENUS MINIMUS MUSCLE*

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MUCH has been written about the "scalenus anticus syndrome". To most surgeons this term has signified a clinical entity resulting from compression of the brachial plexus by the scalenus anterior (anticus) muscle. It has become apparent in recent years, however, that other muscles of the scalene group may be implicated in this symptom-complex. It would therefore seem reasonable to adopt for it a more generic name, such as "scalene syndrome".[8, 12]

The following case illustrates the cure of a long-disabling brachial neuralgia by section of a scalenus minimus muscle.

History.—A pleasant and intelligent housewife, 35 years of age, began, 6 years ago, to experience an aching, hurting pain in the right upper extremity, involving the whole arm, the medial aspect of the forearm, the medial half of the hand and the 3rd, 4th and 5th digits. The pain occurred intermittently, with prolonged periods of freedom. Six months ago it became constant, although varying to some extent in severity. At times it was very intense and completely disabling and when most severe, there was a spread from the arm to the back of the shoulder. Occasionally it was associated with a feeling of numbness and tingling in the medial half of the hand and the corresponding digits. Due to weakness or clumsiness she tended to drop things, so much so that she avoided carrying valuable objects. The pain was worse if she did any hard work involving the use of the right arm, particularly lifting, and, if she used the hand too much, she felt a sharp, though transient, stab in the thumb. She had noticed that the pain was eased by abducting and elevating the arm, and sometimes obtained considerable relief by lying with the arm above the head. More recently she had observed that the right hand was frequently bluish and mottled and, when the colour was most abnormal, she was aware of a throbbing element to the pain. Finally, she had the impression that the right hand and arm perspired more than other parts of the body.

When we first saw the patient, she was upset, nervous and irritable, and was finding it impossible to fulfil her family and household duties. Mild analgesics gave her no relief, though she claimed some benefits from stronger drugs.

Examination.—Intense tenderness could be elicited all over the root of the neck on the right side, and pressure in this area produced pain which radiated through the entire right upper extremity, particularly into the ulnar side of the forearm and hand. Traction downwards on the extremity or shoulder also produced this pain, at the same time causing obliteration of the pulse at the wrist. Neither pain nor obliteration of the pulse occurred on examining the left upper extremity in this way. (However, if no traction was put on the shoulders, the blood pressures in the two arms were scarcely different, being 110/65 on the right and 115/70 on the left). When the right hand was allowed to hang dependent, it rapidly became mottled and somewhat cyanosed.

An extensive sensory loss was demonstrable. This was most marked over the medial side of the forearm and hand, where definite hyperæsthesia as well as analgesia were present, but reduced sensation was witnessed also over the shoulder and on the lateral side of the arm. Vibration sense was less acute on the ulnar side of the hand, and position sense less accurate in the little finger than in the index and thumb. There was no definite motor weakness; though power seemed reduced in biceps, forearm and hand, full effort was not put forth because of pain. In any case there was no measurable atrophy. The deep reflexes of both upper extremities were brisk and equal.

The extent and unanatomical distribution of the sensory deficit was a puzzling feature, but since the boundaries of the hyperæsthetic area were not very constant on repeated examinations and, since good sensation could be elicited even in the centre of this area, it was concluded preoperatively that a strong functional overlay was present. It was fully appreciated that this might account also to some degree for the patient's pain, but that the latter could be purely functional seemed very unlikely in view of the logical history and the objective localized circulatory disturbance.

Investigation.—X-rays revealed neither cervical rib nor abnormality in the cervical spine.

Diagnosis.—The main conditions which had to be considered as a cause for the upper limb pain in this particular case were herniated cervical intervertebral disc, cervical rib, costoclavicular compression and the scalene syndrome. With herniation of a cervical intervertebral disc narrowing of the corresponding disc space (usually C. 5-6 or C. 6-7) is commonly found by x-ray, and, as would be expected, the peripheral distribution of the pain tends to be lateral rather than medial in the forearm and hand. Characteristically, pressure down upon the head aggravates the pain, whereas traction upwards gives relief. In addition, many disc cases have headache as a principal symptom.[11] On none of these counts was a herniated disc implicated in our case, so that myelography was considered unnecessary. Cervical rib was ruled out very simply by x-rays. The costoclavicular syndrome was not definitely eliminated as a possibility, though the more-or-less sedentary (and non-military) occupation of our patient seemed against it. Besides, no asymmetry of the thoracic inlet or of the clavicles was noted radiographically. These considerations, as well as the extreme tenderness in the root of the neck and the primarily ulnar pain and sensory disturbance, plus vascular disturbance in the hand, finally led us to diagnose a scalene syndrome.

Operation.—Operation was done under general anæsthesia. Through a fairly generous incision the scalenus anterior was first exposed and divided. This muscle did not seem to be producing any unusual pressure on the subclavian artery or brachial plexus, so the operation was continued, the subclavian artery being carefully dissected out. Deep to the latter could be seen another well-defined bundle of muscle inserted into the first rib (Fig. 1). When this muscle, the scalenus minimus, was divided, the 8th cervical and 1st thoracic nerves were brought clearly into view. It was apparent that they had been compressed by the minimus as they came together over the first rib to form the lower trunk of the brachial plexus. It was felt that the chief cause of the brachial neuralgia had been found and adequately dealt with.

Course.—Postoperatively the patient did exceedingly well. Sensation began to return to the analgesic area within 24 hours and soon normal feeling was restored throughout. The pain disappeared over a period of days. Especially was the patient pleased when her young son spoke of the doctor as "the man who took the blue colour out of your hand". Six months' postoperatively, though admitting an occasional ache, she claimed complete freedom from her original pain and disability. More important, she was well pleased, easy to live with and in excellent spirits.

ANATOMY

The scalenus minimus muscle is well-known in the anatomical world, and its name (Albinus, Soemmerring) has many synonyms: scalenus

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Fig. 1.—Key structures in the root of the neck in the case reported.

pleuralis (Sibson), muscle suspenseur de la plèvre (Sebileau), petit scalène (Meckel, Bougery), scalenus accessorius (Macalister), scalène intermèdiaire or pleuro-transversaire (Testut), and scalenus anticus minor. Excellent descriptions of the minimus muscle are to be found in the treatises of Le Double[9] and Eisler[4] (Bardeleben), and Todd[14, 15] dealt extensively with its surgical anatomy in his papers on cervical rib. More recently the scalenus minimus has been well illustrated in Grant's[7] atlas.

The scalenus minimus muscle usually arises from the anterior tubercle of the transverse process of the 7th cervical verebra, the origin being partly behind the emerging 7th cervical nerve. However, Todd[15] has noted that the minimus may, at least in cases with cervical rib, descend from the 6th, the 6th and 7th, or the 5th, 6th and 7th cervical transverse processes. It develops in common with the scalenus anterior muscle, in some cases seeming to split off from the latter (which arises as a rule only as low as the 6th cervical transverse process). It passes downwards parallel to the posterior border of the scalenus anterior to insert into the first rib between that muscle and the scalenus medius, the lateral border of origin becoming the anterior border of insertion. In the majority of cases the scalenus minimus lies posterior to the subclavian artery and in front of the lower two roots (anterior primary divisions of C.8 and T.1) of the brachial plexus, as the latter come together to form the lower trunk (Le Double[9]). It may, however, bear a complex relationship to the roots of the plexus, and occasionally it circumscribes the artery as a loop or joins the scalenus anterior tendon beneath the artery. It sends a process (inserting into and contributing to Sibson's fascia) to the pleural cupola which serves to make the pleura tense. According to Sebileau (Eisler[4]) this tensing function is primary, the scalenus minimus forming with the costo-pleural ligament the suspensory apparatus of the pleura. The scalenus minimus muscle is 6 to 8 centimetres in length and variable in thickness. It may be quite fleshy or largely tendinous. If completely atrophied, it is known as the vertebro-costal ligament. It is innervated by the anterior primary division of the 8th cervical nerve.

The scalenus minimus is not a rare muscle. In fact, Sebileau and Le Double[9] consider it to be a constant finding, though sometimes represented only by the vertebro-costal ligament. In any case its absence rather than its presence might be considered anomalous, for Zuckerkandl (about 1877) found it in 22 out of 60 bodies on both sides, 12 times on the right side only, and 9 times on the left (Eisler[4]); thus he showed a subject incidence of 72%, an absolute incidence of 54%. Quite recently Reed and Weed (reported by Gage and Parnell[6]) examined over 100 cadavers, finding the muscle (called the scalenus anticus minor) bilaterally in 25, on the right side in 41 and on the left 39. Kirgis and Reed,[8] in their series of 112 dissections, found the scalenus minimus muscle in 55% on the right side, in 56% on the left; in a further 26% the vertebro-costal ligament was present.

DISCUSSION

In many papers on the scalene syndrome there has been no word of the scalenus minimus, in others the muscle has been mentioned without consideration of its implications.[1, 2] However, at least four papers in the recent literature (Falconer and Weddell,[5] Gage and Parnell,[6] Kirgis and Reed,[8] Rogers,[12] and Telford and Mottershead[13]) have discussed the minimus muscle as a possible factor of importance in the production of the scalene syndrome. One of these, that of Falconer and Weddell, cited a specific case. In the latter (case 4) the abnormal findings were

purely neurological (that is, there was no vascular or neurovascular disturbance) and the patient gave no history of pain. At operation on this man a taut, tendinous band representing the scalenus minimus was found compressing the lower trunk of the brachial plexus against the neck of the first rib. The subclavian artery was not involved. Division of the band, or vertebro-costal ligament, leaving the scalenus anterior muscle intact, resulted in a clinical cure with complete neurological recovery.

In contrast, the findings in our patient included not only neurological but also vascular or neurovascular changes, and pain was her chief complaint. Here again, however, operation revealed a scalenus minimus, in this case a well-developed muscle, and section of this along with the scalenus anterior similarly resulted in cure.

The significance of our patient's circulatory disturbance in terms of cause remains uncertain. Adson and Coffey[2] have pointed out that the vascular changes in cervical rib and scalene syndromes are difficult to explain on one hypothesis, some signs apparently arising from direct and observable compression of the subclavian artery, others from involvement of the sympathetic supply to the peripheral vessels (which joins and travels in the brachial plexus). De Palma[3] believes the latter to be the more important. It may be of consequence that the minimus muscle in our case was large and well-developed. Kirgis and Reed[8] have shown that the width of the scalenus minimus, especially when of good size, may be equal or almost equal to the distance between the attachments of the scalenus anterior and medius muscles to the first rib. In this circumstance the minimus must leave little room between anterior and medius for the subclavian artery in front or the lower trunk of the brachial plexus behind, and would seem to be ideally located to contribute to a double squeeze-play in which both these structures might be trapped. Actually for anatomical reasons the greater squeeze tends to occur behind the minimus, that is between minimus and medius, as was observed in our case. (Both Kirgis and Reed[8] and Rogers[12] have pointed out the strategic significance of the scalenus medius in the scalene mechanism). In view of the operative findings in our patient, it seems likely that interscalene compression gave rise to her symptomatology, the vascular component resulting largely from irritation of or pressure on the sympathetic fibres running with the lower plexus trunk, perhaps also to some degree from direct arterial involvement. That a primarily costoclavicular pinch of the subclavian artery may have been an additional factor is a possibility that cannot be ruled out, as this condition may sometimes be relieved by section of the scalenus anterior muscle (McGowan and Velinsky[10]), a procedure carried out in the present instance.

The widespread distribution of the pain in our patient also requires explanation, but this should not prove insuperable. Deep pain may have three components: that from the primary noxious stimulus, that of referred nature, and that due to secondary muscular contractions (Wolff and Wolf[16]). Possibly in our case spasm involved not only the scalenus minimus but also secondarily other scalene muscles, so extending the neurological disturbance to higher roots. The fact that dermatomes, myotomes and sclerotomes are not accurately superimposed in the shoulder (or in the pelvic) region may also be significant, for involvement of even a single root at either of these levels can give rise to pain of wider distribution than might at first be thought.[16]

SUMMARY AND CONCLUSIONS

1. The importance of the scalenus minimus muscle as a cause of brachial neuralgia has been emphasized.

2. A case has been presented in which a dramatic cure was obtained by section of both the scalenus anterior and minimus. It is felt that the minimus muscle was the primary cause of the disabling upper-limb pain in this particular case.

3. Wide exposure should be made when the root of the neck is being explored for a cause of brachial neuralgia.

ADDITIONAL NOTE.—Following completion of this paper Dr. R. I. Harris has kindly supplied the authors with the history and operative findings in a patient recently under his care. The symptom complex was quite comparable to that described in our patient. At operation Dr. Harris divided both scalenus minimus and medius, but felt that the minimus muscle was the real cause of the pressure on the lower part of the brachial plexus. Following operation the symptoms and signs rapidly cleared up as in our patient.

The authors wish to thank Dr. J. G. Hall, who contributed materially to the neuropsychiatric examination of the patient.

REFERENCES

1. ADSON, A. W.: *Surg., Gynec. & Obst.*, **85**: 687, 1947.
2. ADSON, A. W. AND COFFEY, J. R.: *Ann. Surg.*, **85**: 839, 1927.
3. DE PALMA, A. F.: *Am. J. Surg.*, **76**: 274, 1948.
4. EISLER, P.: Die Muskeln des Stammes, Vol. 2, Sect. 2, Part I, p. 308, in Bardeleben, K. v.: Handbuch der Anatomie des Menschen, Gustav Fischer, Jena, 1912.
5. FALCONER, M. A. AND WEDDELL, G.: *Lancet*, **245**: 539, 1943.

6. GAGE, M. AND PARNELL, H.: *Am. J. Surg.*, **73**: 252, 1947.
7. GRANT, J. C. B.: An Atlas of Anatomy, The Williams and Wilkins Company, Baltimore, 2nd ed., pp. 308 and 415, 1947.
8. KIRGIS, H. D. AND REED, A. F.: *Ann. Surg.*, **127**: 1182, 1948.
9. LE DOUBLE, A. F.: Traites des variations du Systeme Musculaire de l'Homme, Vol. I, p. 160, Schleicher Freres, Paris, 1897.
10. MCGOWAN, J. M. AND VELINSKY, M.: *Arch. Surg.*, **59**: 62, 1949.
11. RANEY, A. A., RANEY, R. B. AND HUNTER, C. R.: *J. Neurosurg.*, **6**: 458, 1949.
12. ROGERS, L.: *Brit. M. J.*, **2**: 956, 1949.
13. TELFORD, E. D. AND MOTTERSHEAD, S.: *J. Bone & Joint Surg.*, **30B**: No. 2, 1948.
14. TODD, T. W.: *J. Anat. & Physiol.*, **45**: 293, 1911.
15. *Idem*: *J. Anat. & Physiol.*, **46**: 244, 1912.
16. WOLFF, H. G. AND WOLF, S.: Pain, Charles C. Thomas, Springfield, Illinois, 1st ed. (Rev.), 1949.

PROLONGED EUPHORIA WITH CORTISONE

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A young woman of 19 was admitted to hospital on September 24, 1946, with rheumatoid arthritis. The family physician had diagnosed rheumatic fever and inflammatory rheumatism in 1945, when she complained of sore feet and an inflamed right index finger. In December, 1944, at seventeen years of age, she first noticed pain and swelling in both feet. In August, 1945, she complained of pain, stiffness and swelling in both hands and she was in bed for six weeks. After discharge from hospital, she started to school but, in May, 1946, again complained of pain, stiffness and swelling in both hands and feet. In July, 1946, on the advice of her doctor she went to bed where she stayed until coming to Banff in 1946.

She presented typical clinical and laboratory evidence of rheumatoid arthritis involving the hands and feet, and from then on until 1951 she spent varying periods at the hospital where she was treated on sound basic lines and was kept from having deformities. Gold treatment was used (lauron) and her progress was fairly satisfactory.

The chief point of interest was the effects of cortisone on her mental condition.

On February 21, she was given 300 mgm. of cortisone and the next day 200 mgm. From that time on she had 100 mgm. daily. Twenty-four hour intake and output was measured and weight recorded daily. On February 26, patient felt much better and improvement continued until March 5.

By February 25, pain, stiffness and swelling had disappeared and on March 6 she was limber enough to touch both great toes to her mouth. She could scarcely remember when before this had been possible. She was very optimistic about her future and told me she had been dancing. On March 13 cortisone was discontinued because of the excessive euphoric effect. On March 19, patient was in a state of ecstasy. We became somewhat alarmed when this effect did not disappear after the drug had been discontinued. Control was difficult. She dolled herself up and raced about the hospital. She was usually in good humour but now she seemed to have lost most of her inhibitions. She wanted to dance and go to parties. Barbenyl quarters four times a day had no effect. She refused to take them as they made her sleep and she did not want to sleep. She was discharged on April 1, when her father came for her.

Nurses' notes written between March 15 and April 1. March 15, laughing and at times excitable. Depressed and miserable at times. March 16, crying and very depressed. March 17, found in the night approaching male corridor. March 18, cheerful and singing. March 20, very restless, refuses to remain in room. March 21, patient miserable and cheerful alternately. March 25, very unco-operative. March 26, appears very flighty at times. She drank water from the flowers. Very unco-operative. Making phone calls. March 28, very excitable, wandering about downstairs and very childish. Making phone calls, speaking in an erratic and foolish manner. Went to hospital movie and then ran about the men's ward annoying the patients. Behaviour is very childish though her disposition is quite agreeable. March 29, excitable, will not stay in her room. Annoying other patients. Very agreeable when corrected. Later making a nuisance of herself, hiding behind doors, and bothering other patients. Very childish. Agreeable when corrected but does not heed. Complains of feeling very exhausted.

March 30, calling to people out of the window. Feet swollen somewhat. . . . Excitable. Fully dressed and trying to sneak down the back stairs to go to the dance. Put back to bed. Very co-operative.

When her father first saw her he came immediately and asked me if I thought the cortisone had in some way taken her back to twelve years of age. He said at the age of twelve she was very clever and brilliant. As she grew older she became dull and unable to learn. He felt that in some way the arthritis was instrumental in holding her back and that cortisone may have freed her mentally and physically from the arthritis state. He said that her mother had been unbalanced mentally when one of their children died. Also, when the patient was 14 years of age, she was somewhat unstable mentally.

During her various visits to this hospital for treatment she has been bright and cheery with the odd fit of mild depression. At times she seemed to be five years younger than her age, was always quite sensible, though rather childish at times.

When discharged April 1, she was acting like a twelve year old. Most of the time according to the nurses' notes she was fairly co-operative and easy to deal with. Mentally she was the same as after her last dose of cortisone on March 13.

There were no other side effects. Intake and output were normal. Chlorides and Co_2 combining power were normal. There was no marked retention or diuresis, and no marked change in weight.

Note.—A follow-up report thirteen weeks later showed that she had regained her normal mental state, and her general condition was excellent. The arthritis was still active.

BIBLIOGRAPHY

1. THORNE G. W. *et al.*: *New England J. Med.*, **242**: 783, 824, 865, 1950.
2. PALMER, W. L.: *Am. J. Med.*, **10**: March, 1951.
3. ROME, H. P. AND BRACELAND, F. J.: *Proc. Staff Meet., Mayo Clin.*, **25**: 495, 1950.

A LATE FOLLOW-UP OF THORACOPLASTIES*

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"THE benefits of thoracoplasty cannot be judged solely by the generally accepted standards relative to cavity closure, disappearance of tubercle bacilli from the sputum, etc. The results must also take into consideration the condition of the patient and whether or not he is restored to economic independence." This quotation from Rubin's *Diseases of the Chest* has led us to discuss the late results of thoracoplasty from this somewhat different angle.

The subject matter for review comprises that group of thoracoplasties carried out at the Central Alberta Sanatorium between the years 1940 and 1945 inclusive. During this period 83 cases were so treated by 260 operative stages.

TABLE I.

THORACOPLASTIES 1940-1945

Total number of cases	83	
Untraced	3	
Postoperative deaths	3	
Subsequent deaths	15	
Unimproved	7	
Economically independent	55	—66%

Table I summarizes our findings. Three cases we have been unable to trace; there were three postoperative deaths, and there have been 15 subsequent deaths. Not all of these 15 cases died of late tuberculosis or its complications. Three died from causes not related to tuberculosis: one as a result of wood-alcohol poisoning, one from a non-tuberculous cerebral abscess, and a third was killed in a tractor accident, seven years after a two-stage seven-rib thoracoplasty. He had remained continually well following operation, and was working full-time until his accident.

The remaining 12 deaths were due to a variety of causes, such as pulmonary hæmorrhage, amyloid disease, contralateral pneumonia, spontaneous pneumothorax in the contralateral side, right heart failure, and coronary artery disease.

Seven cases I have classed as unimproved. Two of these are at present in sanatorium; the remainder are unfit to work or only able to do so little that they cannot be classed as engaged in gainful employment.

The remaining 55 cases—or 66% of the total—can be classed as economically independent. Thirty-seven of these cases—or 44% of the total—have remained continually well since discharge from sanatorium, and the average working date in this group is 21.5 months from time of completion of surgery.

The remaining 18 cases—22% of the total—are in guarded occupations. None of them has been re-admitted to sanatorium because of gross spread of disease, but several have been re-admitted for short periods of observation following pneumonia or other acute respiratory infection.

Table II is an analysis of those cases who underwent surgery during the year 1940.

TABLE II.

THORACOPLASTIES 1940

Total	15
Male	9
Female	6
Far-advanced cases	11
Moderately-advanced cases	4
Re-admissions	9
Postoperative deaths	1
Subsequent deaths	3
Unimproved	1
Economically independent	10

Of the 15 cases, 9 were re-admissions, 11 had previously had pneumothorax, 6 had been submitted to phrenic crush, and 2 had had gold therapy.

In this series there was one postoperative death, seven days after a first stage four-rib thoracoplasty. There have been three subsequent deaths, the details of which are as follows: one patient died two years after thoracoplasty of a cerebral abscess, complicating pulmonary sepsis associated with a blocked bronchus; a second patient was in reasonable health for a period of five years, apart from a basal bronchiectasis on the collapsed side; she died following a pneumonectomy to cure this condition; the third death was due to wood-alcohol poisoning.

One case we have classified as unimproved; he has worked intermittently but at present is reported as dying from chronic nephritis.

The remaining 10 cases are economically independent: this group includes the business manager of the sanatorium, a laboratory tech-

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nician, three office workers, and two housewives, all of whom have remained continually well and in employment. Three of the ten cases are now only able to work in guarded occupations but none have had any spread of tuberculous disease: two are doing office work, and the other is engaged in light farm duties at present.

The thoracoplasty cases of subsequent years are employed in all walks of life: medical orderlies, laboratory technicians, farmers, barbers, clerks, carpenters, insurance agents, a pharmacist, and of course, several housewives, who are maintaining homes and in some cases bringing up families.

From an appreciation of the fact that two-thirds of our thoracoplasty cases are gainfully employed five to ten years after operation, one can conclude that our labours have been rewarded by the saving and prolongation of life and the re-establishment of those patients in employment with resulting independence.

STUDIES ON THE EXCRETION OF CORTISONE AND COMPOUND F USING THE PORTER-SILBER METHOD

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AS a result of the discoveries of the past few years, the measurement of the function of the adrenal cortex and its hormones has become increasingly important in clinical metabolic studies. Because of this, a number of techniques have been developed which are capable of being used in a routine clinical laboratory and which allow one to assess the state of adrenal cortical function of a patient.

One such technique is the measurement of urinary excretion products derived from the adrenal cortex, and various methods have been proposed for extracting these compounds from urine and measuring them by either a biological or chemical assay method. These products may be divided into two major groups, the 17-ketosteroids and the urinary corticoids. The former appear to be mainly derived from androgenic compounds secreted by the adrenal and testes while the latter arise chiefly from the glucocorticoids secreted by the adrenal cortex.

Use of the urinary levels of these groups of compounds as a method of measuring adrenal function suffers from two major disadvantages. One is that the amounts excreted account for only a small fraction of the active hormones produced by the adrenal. The other is that the methods currently in use are relatively non-specific so that many compounds are measured in any particular assay and not all of those measured are related to the active adrenal hormones.

Recently a method for the measurement of corticoids has been described by Porter and Silber[1] which gives promise of at least partially obviating this second difficulty. This method is reported to be specific for a relatively small group of closely related compounds referred to as 17, 21-dihydroxy-20-ketosteroids, a group which includes cortisone and compound F. It is based on a colour reaction formed between these compounds and phenylhydrazine in sulphuric acid. Although the above authors were unable to use their method to detect cortisone in the plasma or urine of a dog after the administration of 100 mgm. subcutaneously, it has been found possible to adapt their method for clinical studies. This article is a preliminary report on the possible value of this method in measuring the excretion of cortisone and compound F activity in urine.

METHOD

Urine was collected with a small amount of chloroform as preservative. It was stored in a refrigerator at 5° C. and the determination carried out usually within a week of the time of collection. (Experiments indicated that longer storage resulted in a loss of active material.) A 125 c.c. aliquot was acidified to approximately pH 2 with 5M sulphuric acid, and extracted by shaking with 75 c.c. of chloroform. The emulsion which formed was broken by centrifugation and the chloroform layer was separated. The extraction was repeated with 50 and 25 c.c. portions of chloroform. The combined chloroform extract was transferred to a separatory funnel and washed once with 15 c.c. of N/10 sodium hydroxide and once with 15 c.c. of water. The chloroform was then taken to dryness under reduced pressure at 40° C. The residue was taken up in 5 c.c. of methanol. A one c.c. aliquot of this solution was used for measurement of 17, 21-dihydroxy-20-ketosteroids as described by Porter and Silber. In some cases where the urine contained large amounts of cortisone-like compounds, the dilutions were adjusted so that the optical density readings were not greater than 0.8.

* Holder of a Medical Research Fellowship administered by the Canadian Life Insurance Officers Association. This work was also supported in part by the National Research Council of Canada.

A standard curve was prepared as follows: A cortisone suspension (Cortisone Acetate—Merck—5 mgm./c.c.) was diluted 20 times with physiological saline, and 0.25 to 1.25 c.c. portions of the diluted solution were added to 125 c.c. aliquots of a pooled sample of urine. These were then extracted by the procedure already outlined and the residue from the chloroform made up in 5 c.c. of methanol, of which a one c.c. aliquot was used for the colorimetric determination. Since control urines contain small amounts of material which give a colour with this test, an aliquot was also extracted without added cortisone to give a control value, which was then substracted from each of the other values obtained. A standard curve was also prepared using a suspension of compound F (17-hydroxycorticosterone-21-acetate-Merck-25 mgm. / c.c.). The results are shown graphically in Fig. 1. Extraction of cortisone and compound F from urine by this method was found to be nearly quantitative.

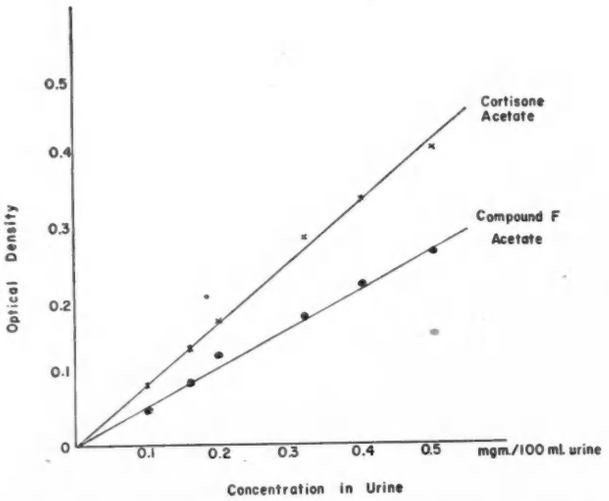

Fig. 1.—Standard Curves. Optical density actually refers to the difference in optical density (a—b) described by Porter and Silber, where b is a blank reading to allow for urinary pigments and other compounds which give colours in the sulphuric acid medium both in the presence and absence of phenylhydrazine.

RESULTS

Excretion of orally administered cortisone.—The method described has been used to study the rate and total amount of excretion of orally administered cortisone and compound F in man. Urine was collected from three normal adult males for an initial three hour period which served as a control. They were then given 100 mgm. of cortisone orally, (25 mgm. tablets of cortisone acetate—Merck) and the urine collected for four more three hour periods and finally for a twelve hour period, making a total of 24 hours after administration of the cortisone. This experiment was repeated at intervals of a week or more on the same three individuals, using different doses of cortisone. It was also repeated on two of the three, using a 50 mgm. dose of compound F (saline suspension of 17-hydroxycorticosterone-21-acetate-Merck-25 mgm. /c.c.). The results are shown in Fig. 2 and Table I.

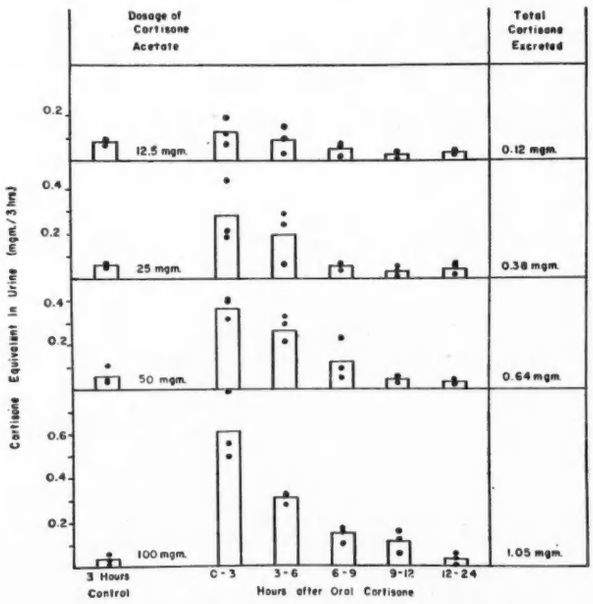

Fig. 2.—Excretion of a single oral dose of cortisone in normal individuals. The cortisone equivalent was calculated from the standard curve prepared with cortisone acetate (Fig. 1). The height of the columns represents in each case the average of three determinations. The individual values are indicated by dots.

The total amount of cortisone excreted is calculated as the amount excreted in excess of the normal base level.

From these results it may be seen that normally the excretion of these compounds is at a low level. Following the oral doses of cortisone

TABLE I.

EXCRETION OF A SINGLE ORAL DOSE OF 50 MGM. OF COMPOUND F IN NORMAL INDIVIDUALS

Subject	*Control 3 hours*	*Amount excreted (mgm./3 hours)* 0–3	3–6	6–9	9–12	*12–24 hrs. after compound F*	*Total amount excreted (mgm.)*
1	.03	.69	.49	.05	.17	.02	1.04
2	.09	1.33	.27	.06	0	.01	1.52

The amount excreted was calculated from the standard curve prepared with compound F acetate (Figure 1.). The total amount excreted was calculated as the amount excreted in excess of the normal base level.

and compound F there is a sharply increased excretion, the highest level being attained during the first three hours. Furthermore, the total amount excreted is related to the amount administered. Administration of cortisone either before or after a meal seemed to make no difference to the rate of excretion or the amount excreted.

The urinary excretion of cortisone has also been followed on a number of patients receiving daily therapy of oral cortisone for rheumatoid arthritis. The results obtained on two such patients are shown in Fig. 3. Both of these patients had been arthritics for several years and both had had several previous courses of ACTH or cortisone therapy. The cortisone was given in equal divided doses at 6 hour intervals for the first ten days, and then at 6 and 12 hour intervals depending on the patients' requirements.

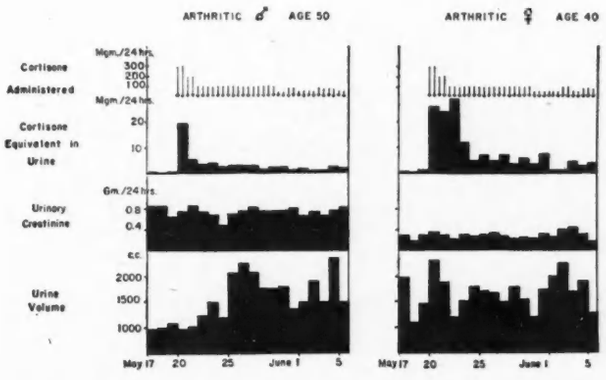

Fig. 3.—Excretion of oral cortisone in patients with rheumatoid arthritis. The cortisone equivalent was calculated from the standard curve prepared with cortisone acetate (Fig. 1).

There was a marked difference shown in the amount of cortisone excreted by these two patients although both received approximately the same dosage. Both improved with therapy and both were eventually stabilized at approximately the same dose level.

Excretion following ACTH therapy.—A compound or compounds which give a positive test in the Porter-Silber reaction appear in the urine following therapy with ACTH. The effect of such therapy on a 15 year old boy treated for purpura hæmorrhagica with ACTH is shown in Fig. 4. The amount of chromogenic material in the urine was greatly increased from the third day of ACTH therapy, but decreased rapidly when the treatment was discontinued.

The stress and shock associated with a major operation likewise produced an increase in chromogenic material in the urine of several patients. The results from one case (adult male—gastrectomy) are also included in Fig. 4. It should be stressed that these are preliminary results and it is not intended that direct comparisons should be made between the actual increases in cortisone-like material in the urine following ACTH therapy and that following an operative procedure.

Excretion values in normal and pregnancy urine.—Reference to Figs. 2-4 shows that the control urine samples contained small amounts of 17, 20-dihydroxy-20-ketosteroids. In order to obtain further information regarding the amounts of these compounds in normal urine, the Porter-Silber reaction was applied to ex-

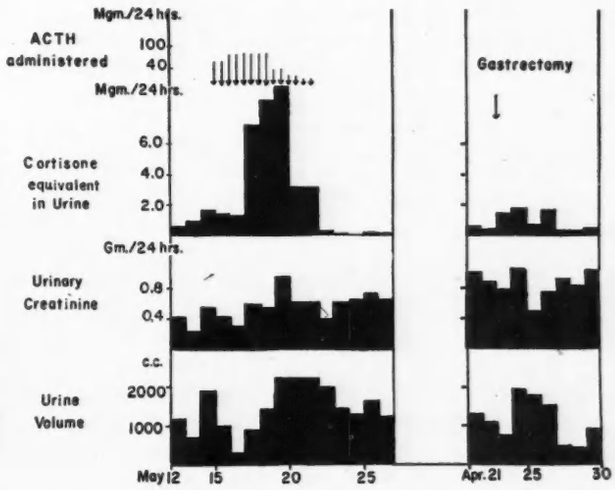

Fig. 4.—Excretion of 17, 21-hydroxy-20-ketosteroids following ACTH therapy and after surgery. The cortisone equivalent was calculated from the standard curve prepared with cortisone acetate (Fig. 1). Note that the scale is not the same as that in Fig. 3.

tracts of the urine of 8 adult males and 7 adult females. For males, the cortisone equivalent ranged from 0.10 to 0.40 with an average of 0.25 mgm./24 hours for 11 determinations. For females, the values ranged from 0 to 0.86 with an average of 0.24 mgm./24 hours for 14 determinations. Five of the 14 were negative values. In 5 cases studied in the third trimester of pregnancy, the highest value was 0.84, the average value 0.36 mgm./24 hours and two of the five urines gave negative results. The significance of these values are being studied further.

Excretion in other species. Dog.—Porter and Silber reported that they were unable to detect 17, 21-dihydroxy-20-ketosteroids in the plasma or urine of a dog following the subcutaneous injection of 100 mgm. of cortisone acetate. Repetition of this experiment using the technique as described, however, showed that the injection of such

a dose of cortisone acetate resulted in the excretion of the equivalent of more than a millegram of cortisone during the succeeding 24 hours. Several control specimens of dog's urine gave negative results with this test.

Rat.—A somewhat more detailed study of the excretion of orally administered cortisone has been carried out in the rat. The data is presented in Table II. Cortisone tablets were powdered, suspended in water and administered to rats by stomach tube. Two rats were used in each test and the excreta were pooled. In some cases the rats were fasted for 24 hours before the cortisone was administered. Fæces and urine were collected for 48 hours after the cortinsone was given, but in all cases it was detected only during the first 24 hour period.

Extraction of the dried fæces was performed by grinding them in a mortar with successive portions of chloroform. This relatively crude method gave only 50% recovery of cortisone added to fæces from untreated rats, so that the results in Table II are only a rough approximation of the amount of cortisone excreted. In later experiments, it was found that extraction of the fæces with chloroform in a Sohxlet gave a recovery of 80% or better of added cortisone.

TABLE II.

EXCRETION OF ORAL CORTISONE IN RATS

Average body weight (gm.)	*Dosage of cortisone (mgm.)*	*Cortisone equivalent excreted*	
		Fæces (mgm.)	*Urine (mgm.)*
—non-fasted rats—			
195	25	0	
208	50	4	
—rats fasted 24 hours—			
209	25	6	less than 0.3
208	50	16	1.0
197	100	35	less than 1.0

From these results it appears that when very high doses of cortisone acetate are given to rats orally, a large proportion is excreted in the fæces. It seems probable that the material excreted has passed through the intestine without ever having been absorbed. It should be noted that a relatively larger proportion was excreted in the rats that were fasted.

DISCUSSION

The method which has been described appears to have considerable merit in the quantitative assay of urinary cortisone and related compounds. Measurable increases in such compounds have been obtained consistently following the administration of cortisone, compound F, and ACTH, and the amount of the increase has been directly related to the dose administered in normal individuals. This method has the advantage that it is less time-consuming than other methods, and it may prove to be more specific for active steroid hormones than some of the other chemical assay methods that have been proposed. In this connection further tests with the phenylhydrazine-sulphuric acid reagent on other steroids would be of value.

Mason[2] has shown by actual isolation studies that when cortisone is administered to patients, small quantities are excreted unchanged in the urine. The data presented in this paper give a picture of the rate and amount of excretion of this compound following a single oral dose. It would appear from the high excretion value during the first three hours that the compound is not only rapidly absorbed from the gut, but is readily lost through the kidneys. Since the same pattern of excretion is shown for all doses of cortisone from 100 mgm. down to 12.5 mgm. it is suggestive that the kidney threshold may be low and that the substance is present in the blood for only brief periods following a single oral dosage. Although the excretion may remain slightly elevated for 12 hours it would seem that utilization or destruction of cortisone is rapid. It is of interest that in the experiments described, the cortisone was taken in some cases after a heavy meal. Despite this, the excretion peak was in the first three hours. An extension of these observations may be of value in explaining the reported discrepancy in the therapeutic results of oral cortisone[3] and lead to the establishment of an optimal dosage schedule.

Surgical intervention as well as ACTH was found to result in increased excretion values by the test described. Mason was able to isolate compound F, but not cortisone, from the urine of patients receiving ACTH, so it seems likely that compound F is responsible for most of the increased value obtained with the Porter-Silber colour reaction following the administration of ACTH and also, presumably, in postoperative patients.

It should be noted that a given optical density in the Porter-Silber reaction corresponds to a somewhat greater amount of compound F acetate than of cortisone acetate (Fig. 1).

The values obtained in normal urines are somewhat lower than those obtained with other chemical methods of measuring urinary corticoids. This may mean that the present method is more specific for active adrenal hormones. However, in some cases negative results have been obtained and the low levels present in normal urines approach the limit of accuracy of the method. Further, as Porter and Silber have pointed out, the presence of appreciable quantities of some other steroids (*e.g.*, pregnenolone) could lead to high blank values and so introduce an error.

Other studies have suggested that the increased urinary corticoids in pregnancy are derived from sources other than the adrenal.[4] The fact that negative results were obtained with two pregnancy urines using the present method suggests the possibility that the increased corticoids in pregnancy urine measured by other methods[5] may be substances other than cortisone or compound F. In view of the clinical improvement observed in arthritic patients during pregnancy, further study of their urinary corticoids is indicated.

The experiments described indicate that following cortisone administration to a dog, appreciable quantities are excreted in the urine. Similarly in the rat, urinary excretion occurs. The possibility of non-absorption of oral cortisone from the gut has not yet been investigated in humans. In the rat, however, large doses of cortisone (up to 25 mgm.) may be given before tests on the extracts of fæces become positive. Very massive oral doses in the rat may be followed by the appearance of appreciable quantities in the fæces, presumably as a result of non-absorption.

SUMMARY

The colour reaction described by Porter and Silber and reported to be specific for cortisone and related 17, 21-dihydroxy-20-ketosteroids has been successfully applied to the measurement of such compounds in urine. Preliminary observations have shown that small amounts are present in most normal urines, and consistent increases have been observed following oral administration of cortisone and compound F, injection of ACTH, and after major surgical operations.

This method is less time-consuming than other similar methods, and is relatively simple, and yet appears to be specific for active adrenal hormones and their metabolites. Further studies on cortisone, ACTH, and the assessment of adrenal cortical function using this method are under investigation.

The authors wish to thank Dr. J. B. Collip for initiating this study and for his continued interest in the experimental results. They are also indebted to Misses C. Drulard, B. Byrns, and F. Sayers and to Mr. E. Andersen for valuable technical assistance.

The cortisone acetate and compound F acetate used in these experiments were generously donated by Dr. J. M. Carlisle, Medical Director of Merck and Co., Inc., Rahway, N.J. The pregnancy urines were obtained through the co-operation of Dr. G. R. Girvan.

REFERENCES

1. PORTER, C. C. AND SILBER, R. H.: *J. Biol. Chem.*, **185**: 201, 1950.
2. MASON, H. L.: *J. Biol. Chem.*, **182**: 131, 1950.
3. BOLAND, E. W. AND HEADLEY, N. E.: *J. A. M. A.*, **145**: 8, 1951.
4. JAILER, J. W. AND KNOWLTON, A. I.: *J. Clin. Invest.*, **29**: 1430, 1950.
5. VENNING, E. H.: *Endocrinology*, **39**: 203, 1946.

THE TREATMENT OF VARICOSE VEINS

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VARICOSE veins have been treated haphazardly and irrationally at times and the results have left much to be desired.[14, 43, 45] It is because of the difficulty and complexity of this problem and the belief that the methods used to date are ineffectual and ofttimes harmful to the patient that this paper is submitted. A complicated ritual[3, 9, 22, 28, 29, 42, 45, 46, 47, 50, 52] has been developed to assess the status of the venous circulation in the lower limbs. It is true that the process which has led to the development of the varicose veins is difficult to disentangle, but it is the proper elucidation of the sequence of events and the determination of the sites of failure of the system which are of utmost importance in applying rational treatment.

The local treatment of varicose veins by surgical procedures has led to almost innumerable methods, most of which have been unsatisfactory. The surgical treatment of varicose veins is not easy. There is no sure-fire, simple and completely safe operation, and the present day tendency to attend these "miserable" patients in the outdoor or office with inept operations or injections on the expedient of economic necessity is both dangerous and worthless.

The surgical treatment may be considered to fall into three major groupings, many of which are to be combined. (a) High sapheno-femoral vein ligation, (b) the use of sclerosant solutions (c) removal of the superficial varices by excision or stripping. Other measures may be required as well, such as sympathetic blockade, methods of treatment of lymphœdema, superficial femoral vein ligation[32] and popliteal vein ligation[4] and other régimes required or advo-

cated in the treatment of varicose ulceration. Of these latter means little will be said at the present time.

HIGH SAPHENO-FEMORAL VEIN LIGATION

Numerous papers[9, 16, 17, 20, 22, 28, 29, 30, 42, 45, 52] have been previously presented in the technique of high saphenous ligation and all its branches. In the primary type of varicose veins and in those in which the incompetence of the venous system is confined to the long saphenous portion, high sapheno-femoral vein ligation improves the situation markedly. This can be done by itself, or in combination with the use of sclerosant therapy or excision therapy. It may be badly performed[42] and this may lead to a failure to control the reversed blood flow and the development of so-called recurrence of varicose veins.[9, 41, 42, 43, 49] The irregular anastomotic arrangement of the long saphenous and its tributaries in the groin[13] (it can differ on the two sides markedly in the same individual) explains the almost universal belief that recurrence of varicose veins following a past high sapheno-femoral ligation can lead to re-exploration and the finding of communicating channels to the long saphenous system, and it has been the experience of many surgeons[28, 42] to re-operate in the area of the fossa ovalis and find communication with pudendal, circumflex iliac or accessory saphenous veins. The proper performance of a high sapheno-femoral ligation is not an easy procedure. It must not be done through a small incision and the type of exposure is of some importance. It is believed that the most satisfactory incision is a vertical one parallel (slightly medial) to the femoral vessels. Meticulous dissection must be done, with individual ligation of the vessels. The dangers are hæmorrhage[39] and the blind clamping of vessels with attendant risk of injury to the femoral artery[35] or femoral vein. Men of experience have sectioned the femoral artery in error, and in a few reported instances, actual injection of sclerosant material has been done with subsequent loss of limb.[35] This is a fearsome problem and one which should be duly recognized.

A further troublesome feature of this operation is persistent lymphorrhœa and often this is complicated by secondary infection from manipulation of the superficial inguinal lymph nodes which are the seat of a low grade infection. This is more apt to occur in those who have an actual focus of infection in the regions which are drained by these lymph nodes, such as an active infected ulcer.[34] Therefore, it is submitted this operation should be deferred until such time as the acute inflammatory phase of the ulceration is under adequate control and proper aseptic technique can be carried out. With the modern use of antibiotics the dangers of infection can be minimized and one makes it a routine practice to use antibiotics in the preoperative preparation of the patient even when an ulcer is healed. It is this danger of infection in the groin which would suggest the use of an absorbable suture material to minimize the risk of sinus formation. In performing this procedure due care should be made to tie off the saphenous vein flush with the femoral vein and transfixion distally is a simple precautionary step. Ligation in continuity of the saphenous vein is considered worthless. Preferably a segment of saphenous vein is excised, and it affords one the opportunity to seek and ligate an accessory saphenous vein which is found in the majority of limbs.

This operation is a good procedure and in many instances will control the large tortuous varicose veins seen in individuals who have varicose veins without evidence of deep venous incompetence. It can be combined with multiple ligation of communicating veins[22, 45, 46] or with removal of small segments of the saphenous vein. The difficulty with this latter procedure is the number of incisions (as many as thirty in a limb), and the failure to identify and locate all the communicating channels present. One has diligently applied all available measures (Pratt test, venograms) and still failures resulted. Nevertheless, it is as good as can be done short of excision.

SCLEROSANT THERAPY

The use of sclerosants is an old procedure. It was first introduced by Pravaz in 1851[48] when he attempted to cure an aneurysm with a ferric chloride solution. This led to the development of injection treatment for a wide variety of pathological lesions and was particularly used for the treatment of varicose veins (and hæmorrhoids), being popularized in the late 1920's and early 1930's with the development of such sclerosants as sodium morrhuate by Wright.[48] Numerous other sclerosants[42] were developed, such as Genevrier's solution (quinine 12% and urethane ethyl carbonate 6%), 50%

dextrose, 30% sodium chloride and more recently, sodium tetradecyl sulphate.[11, 15, 26] The use of these materials depends on an irritation of the intima of the vein and the development of a chemical thrombosis, and finally fibrosis and obliteration of the vessel lumen. Numerous methods of technique were developed with performance of orthograde, retrograde, horizontal and vertical injection, with and without a tourniquet, with injection in the elevated position and replacement of the limb in a dependent position, all fancy methods depending on the ingenuity and likes of the individual operator. The most commonly used material has been sodium morrhuate (more recently sodium tetradecyl sulphate) because there were several objectionable features to most of the other materials and it was felt by most men that the use of sodium morrhuate was a relatively simple, benign procedure with a morbidity and mortality that was essentially very low. Its advocates claimed it to be adaptable to office and outpatient use, relatively economic, and tolerated in the main by most patients. The difficulties have been immediate local and general reactions, and latent local and general reactions. It is amazing however, how difficulties in its use have been passed over, particularly the fact that injury to the patient leading to stasis dermatitis and varicose ulceration has been seen (Case 1 and 2 are examples).

CASE 1

J.H.M.L., aged 60, male. History of varicose veins since 1917. Treated by several injections in 1934. Was troubled with swelling of the legs following the last injection (sodium morrhuate 1 c.c.), pain, blueness and inability to walk. Recovered spontaneously, but was left with recurrent swelling and pain in the legs. In 1937 he had an appendectomy complicated by a "pneumonia" (cough with bloody sputum), and pleural effusion. Varicose veins recurred with ulceration about the malleoli on both legs requiring repeated hospitalization, periods of bed rest, elevation of limbs and chronic debility. In 1947 he had a right sapheno-femoral vein ligation with ligation of several "blowout" veins and this was complicated by a further pulmonary embolism. Since that time he has been treated with elastic stockings, priscoline, and general measures, but he remains a pernicious economic and medical problem.

CASE 2

T.C., male, age 54. Symptomless veins noted in both legs halfway to knees in 1942. Was in the army on guard duty and following prolonged standing he would note puffiness at the ankles at the end of the day (relative deep venous insufficiency?). In February, 1945, bilateral high sapheno-femoral vein ligation with retrograde injection of sodium morrhuate (5 c.c. of 2½% sodium morrhuate) was done. Immediately postoperatively he had pronounced swelling of the left leg, foot and toes, with blueness, "coldness", and severe pain. Was hospitalized for six weeks. On standing up his discomfort was made worse and he complained of a "bursting pain" in the left leg. Finally out of bed in May, 1945. In August, 1945, he was readmitted to hospital and the left long saphenous at the knee was ligated and he had a further injection (!) below the knee. His temperature was elevated for three days and he had severe pain in th leg and calf on walking. Four weeks later he still had a painful left leg, with puffiness about the ankle, and tired easily. In February, 1948, he had aching pain in the legs at night with moderate varices noted. In March, 1949, telangiectasia, varicosities showing retrograde pressure wave, swelling, cutaneous thickening and pigmentation were noted. Treatment at the present time is with tensor bandages only.

Recently it was pointed out by Boyd and Robertson[6] that there was a great danger in the use of large quantities of sclerosants to the deep venous system, and by special venographic studies[31] it was demonstrated that mass retrograde injection is inaccurate, and that there is rapid dispersal of the injected sclerosant into the deep venous system. Injection of more than 1 to 1½ c.c. results in a rapid overspill of the injected materials into the deep veins and if one recognizes the chemical phlebitis that one produces in the superficial veins, one can well imagine what must happen to the valves of the deep venous tree which act as way-stations for the return of blood to the heart. The maximum site of damage to the deep venous tree undoubtedly must occur at the valves[4] and incompetence of the deep venous valves and communicating valves results in the so-called "recurrence" of varicose veins[40] following either mass or individual injection therapy.

It may be argued by many that this procedure has been done to thousands of individuals with satisfactory obliteration of the superficial varicose veins. The explanation of the variability in the result depends on the number of valves the patient has been endowed with, the amount of damage, if any, to the deep venous tree that has occurred in the past from previous thrombosis, and the amount of sclerosant agent used. In other words it is the cumulative effect on the total efficiency of the deep venous route which determines whether or not there is a recurrence of superficial veins, and with the cases one has observed and the report of the careful follow-up performed by Robertson,[43] one is forced to conclude injection treatment is ineffective and may be dangerous. Hanschell[25] feels that thrombosed varicose veins following sclerosant therapy seldom fail to be completely recanalized, though it may take many months to do so, and concluded that if proper follow-up were carried out injection

therapy would be abandoned, on this acount alone. Anning[2] has stated that the concentration on treatment of superficial varicose veins in patients with ulceration is neither rational or useful and that the results were appalling in several instances.

It is not intended to attribute all the bad results of treatment of varicose veins, such as ulceration, to the use of sclerosant agents, but it is one's contention that sclerosants are dangerous materials, and that the danger of thrombosis to an individual is sufficiently great without introducing a substance known to produce intimal and consequent vascular damage. One cannot tell in advance by ordinary clinical means, other than a strong familial history of varicosis, how much protection the patient has in the number of valves available to carry the load. Anyone who has performed venographic studies is amazed at the rapidity with which the injection of radiopaque media into a superficial vein disperses into both superficial and deep venous systems, and one can well imagine what occurs with the injection of sclerosant materials. Sir Heneage Ogilvie has stated:[41]

> "The injection treatment has no place in the Services; indeed, I would go further and say the time has come to consider seriously whether the injection treatment of veins has any place in legitimate therapy. For those who would dally on the slippery slopes of cosmetic surgery it has its attractions, for it is a cosmetic procedure and no more. The injection of a prominent vein will cause that vein to disappear, but it does nothing to relieve the back-pressure that made it appear in the first place. The same back-pressure will soon dilate another collateral vein, which will in turn be attacked by the injecter, till finally all veins in the leg, including many of the deep ones, are destroyed and the patient is left with a heavy aching, and œdematous limb".

There have been isolated reports scattered throughout the literature of instances of pulmonary embolism and even death following the use of sclerosant agents[24, 35, 39, 51] but it is not these dramatic complications which are of importance, but rather the minor difficulties[8, 38] and the development of postphlebitic ulceration[2, 4, 32, 33, 34, 40] which terminates in a distressing problem to both patient and doctor. It is therefore argued that the use of sclerosants is haphazard, dangerous and the effect nonlasting and that complete cessation of their use be practised by all interested in varicose veins. If a patient is having symptoms sufficient to warrant treatment, ligation and excision are the methods of choice, or in minimal cases, nothing is preferable to the risks incurred with sclerosants. One is convinced that if all who read this will cast back over the cases they have injected, they will come up with one or more instances in which a deep phlebitis has resulted in a "millstone about their neck".

STRIPPING OR EXCISION OF VARICOSE VEINS

This is a method of moderate antiquity[21] and has been practised sporadically for years. It was in vogue in the early part of the century and was given up because of the complexity and difficulty of the procedure, the morbidity associated with the operation, the incidence of infection, and failure to perform adequate high ligation. As well cases were not selected too carefully and the understanding of the pathology was in its infancy. Excision therapy nevertheless was quite effective and from that to stripping of varicose veins was a short step. External strippers, such as the Mayo type stripper, or internal stripping by use of the Babcock (rigid) instrument have recently been re-introduced. Linton[32] used a malleable stripper and more recently, a refinement, the Crystal stripper (Fig. 1) has been a major advance in the treatment of varicose veins.

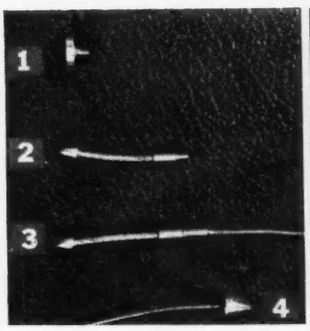

Fig. 1

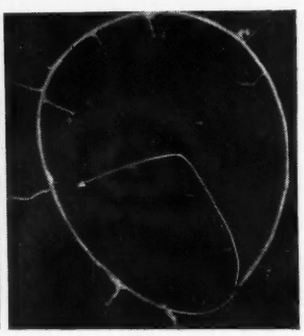

Fig. 2

Fig. 1.—Component parts of the Crystal stripper. (1) The "button" which replaces the malleable wire tip; (2) the small tip is shown attached to the semi-rigid stripper, (3) and (4) shows the Babcock head on the other end of the stripper. The stripper should be long enough to reach from toes to groin, though shorter ones can be used to strip the lesser saphenous vein, or short segments of accessory saphenous veins.

Fig. 2.—This shows a complete stripping from ankle to groin. On the right there is the end of the stripper to which the proximal portion of the long saphenous is attached (the button was removed prior to the photograph being taken) and it shows seven communicating branches in the thigh, and the remaining communicating branches in the leg and calf, down to the ankle.

It consists of a malleable stainless steel wire with a mobile tip which can be slipped around the tortuous portions of the saphenous vein, being introduced in a small cut down incision at the ankle, and brought out, in favourable circumstances, in the groin incision (a sapheno-femoral vein ligation is done prior to the stripping). The moveable tip is replaced by a metal "button" to which the vein is snugly tied, and one then pulls out

the stripper from below, causing the vein to "bunch up" against the "button", therefore increasing the efficiency of the stripping. It has been found that this is more effective than turning the vein inside out, as occurred with ordinary strippers, or polythene rod vein strippers,[10] as the vein tended to break at the site of a communicating vein. In a fairly high percentage a full stripping can be achieved and when one straightens out the vein on the stripper (Fig. 2), one will be amazed at the number of communicating veins hanging on to the main stem. One has found as many as eight communications in the thigh, when one could only determine two by clinical means, and this adequately demonstrates the reason for failure of multiple ligations.

This operation is of fair magnitude and requires hospitalization of the patient. The procedure is usually done under spinal anæsthesia, though it has been done under general anæsthesia. The patient is prepared from groin to toes and draped adequately and is placed in slight Trendelenburg for a few minutes prior to the introduction of the stripper. Bleeding following stripping is relatively easily controlled by simple pressure and elevation of the limb, and after closure of the wounds an elastoplast or other form of compression dressing is applied from toes to groin. Considerable bruising of the tissues frequently occurs, but it is amazing the relative freedom from discomfort that occurs when one has the patient ambulatory following recovery from anæsthesia. The rule of ambulation is five minutes walking every hour during the waking period, though it is not stressed that the patient get out of bed providing adequate foot and leg exercises are carried out assiduously while in bed. Rarely has ambulation been delayed more than 24 hours. Antibiotics are used for three days as a rule, and the average hospital stay has been three days. Prior to discharge the elastoplast dressing is removed and replaced with a two-way stretch elastic bandage from toes to knee which the patient wears while weight-bearing. The elastic support is required for a further ten to fourteen days in the average case, and one finds the bruising and staining cleared in five to six weeks. Any small secondary varices remaining may require ligation which can readily be done under local anæsthesia.

In all cases due attention should be paid to the lesser saphenous vein[7] which can be readily stripped by making a small transverse skin crease incision behind the lateral malleolus (avoid the sural nerve), locating the vein, introducing the stripper and then cutting down on the tip behind the knee, when one feels it dip down into the popliteal fossa. The vein proximally should always be ligated and transfixed.

In order to adequately outline and "mark" the venous system, various dyes have been used. The most efficient "marking" agent has been Brazilian dye (a black leather stain) which is easily obtained at any cobblers. This is painted on over the veins as seen or felt, with the patient upright, the day before operation, and it will last through the ordinary preparation and painting required by aseptic standards.

In some instances it is found impossible to pass the stripper beyond short distances (usually found in patients previously treated by injection therapy, or with very tortuous vessels). In these circumstances "cut downs" can be made to the site of blockage and the short segments stripped, with introduction of the stripper again higher up, or from above downwards. Occasionally one may have to ligate the vein only. In rare cases one may find it necessary to excise huge clusters of veins and this is done by appropriate incision and exposure. This is preferable to useless efforts to pass the stripper.

Sutures are removed on the eighth to tenth postoperative day, and the care of wound is standard for any operative procedure.

SUMMARY

The treatment of varicose veins is difficult. It is not without danger and due care must be exercised at all times in carrying out treatment. It is submitted that a careful history and physical examination are of paramount importance in applying rational treatment. Treatment should be designed to overcome the sites of failure of the venous system in the lower extremities so that appropriate interruption or removal of involved segments of the venous system may be done.

It is contended that sclerosant therapy is a dangerous form of treatment and that its use should be abolished, for it is a cosmetic procedure, and at that of no lasting value.

The treatment of choice at this time we consider to be properly performed high saphenofemoral vein ligation with stripping, using the Crystal modification of the Linton stripper. Treatment should not be performed in the presence of active ulceration.

Medical measures are of major value and should be used in conjunction with surgical means at all times.

We wish to thank Dr. Dean Crystal of Seattle, Washington, for his demonstration of the use of the stripper, and for his permission to publish our support of this method of treatment. Acknowledgment is also due Mr. William Grant of the Department of Photography, Shaughnessy Hospital, Vancouver, B.C., for Figs. 1 and 2.

REFERENCES

1. ALLEN, E. V., BARKER, N. W. AND HINES, E. A.: Peripheral Vascular Diseases, W. B. Saunders, Philadelphia, p. 650, 1946.
2. ANNING, S. T.: *Brit. M. J.*, **2**: 458, 1949.
3. BARONE, A. M.: *J. A. M. A.*, **131**: 1406, 1946.
4. BAUER, G.: *J. International de Chirurgie*, **8**: 937, 1948.
5. BOONE, J. A. AND SMITHY, H. G.: *Ann. Int. Med.*, **31**: 513, 1949.
6. BOYD, A. M. AND ROBERTSON, D. J.: *Brit. M. J.*, **2**: 452, 1947.
7. CARROLL, W. W.: *Arch. Surg.*, **59**: 578, 1949.
8. CATTELL, R. B.: *Surg. Clin. North America*, p. 1445, 1929.
9. CHRISTOPHER, P.: Minor Surgery, 4th ed., Philadelphia, 1941.
10. COLE, J. W. AND HOLDEN, W. D.: *Surgery*, **27**: 280, 1950.
11. COOPER, W. M.: *Surg., Gynec. & Obst.*, **83**: 647, 1946.
12. CURTIS, A. C. AND HELMS, R. W.: *Arch. Dermat. & Syph.*, **55**: 639, 1947.
13. DASELER, E. H., ANSON, B. J., REIMANN, A. F. AND LINDSAY, E. B.: *Surg., Gynec. & Obst.*, **82**: 53, 1946.
14. DE TAKATS, G.: *J. A. M. A.*, **96**: 1111, 1931.
15. DINGWALL, J. A., LINA D. T. W. AND LYON, J. A.: *Surgery*, **23**: 599, 1948.
16. EDWARDS, E. A.: *Surg., Gynec. & Obst.*, **59**: 916, 1934.
17. EDWARDS, E. A. AND ROBUCK, J. D., JR.: *Surg., Gynec. & Obst.*, **85**: 547, 1947.
18. EGER, S. A. AND CASPER, S. L.: *J. A. M. A.*, **123**: 148, 1943.
19. FOOTE, R. R.: *Practitioner*, **158**: 60, 1947.
20. *Idem*: *Practitioner*, **160**: 386, 1948.
21. *Idem*: Varicose Veins, Butterworth & Co., London, p. 16, 1949.
22. GARBER, N.: *J. Internat. Coll. Surg.*, **12**: 531, 1949.
23. GLASSER, S. T.: *New York State J. Med.*, **49**: 1923, 1949.
24. GLICK, M. J.: *J. A. M. A.*, **109**: 300, 1937.
25. HANSCHELL, H.: *Brit. M. J.*, **2**: 630, 1947.
26. HIRSCHMAN, S. R.: *New York State J. Med.*, **47**: 1367, 1947.
27. HOJENSGARD, I. C. AND STÜRUP, H.: *Acta Chir. Scandinav.*, **99**: 133, 1949.
28. HOLLAND, G. A.: *Canad. M. A. J.*, **49**: 184, 1943.
29. HOMANS, J.: *Surg., Gynec. & Obst.*, **22**: 143, 1916.
30. JOHNSTON, C. H.: *J. A. M. A.*, **109**: 1359, 1937.
31. KINMOUTH, J. B. AND ROBERTSON, D. J.: *Brit. J. Surg.*, **36**: 294, 1949.
32. LINTON, R. R. AND HARDY, I. B., JR.: *Surgery*, **24**: 452, 1948.
33. LISKER, S.: *Sur. Clin. North America*, p. 5555, 1947.
34. LUKE, J. C.: *Canad. M. A. J.*, **61**: 270, 1949.
35. LUKE, J. C. AND MILLER, G. G.: *Ann. Surg.*, **127**: 426, 1948.
36. LYALL, D.: *Surg., Gynec. & Obst.*, **82**: 332, 1946.
37. MAYERSON, H. S., LONG, C. H. AND GILES, E. J.: *Surgery*, **14**: 519, 1943.
38. MCCASTOR, J. T. N. AND MCCASTOR, M. C.: *J. A. M. A.*, **109**: 1799, 1937.
39. MUNRO, J. A.: *Canad. M. A. J.*, **60**: 504, 1949.
40. OCHSNER, A. AND DEBAKEY, M.: *J. A. M. A.*, **139**: 423, 1949.
41. OGILVIE, SIR W. H.: *Brit. M. J.*, **1**: 622, 1945.
42. PRATT, G. H.: Surgical Management of Vascular Diseases, Lea & Febiger, Philadelphia, p. 299, 1949.
43. ROBERTSON, H. F.: *Canad. M. A. J.*, **57**: 455, 1947.
44. SCHATKEN, R. V.: *New York State J. Med.*, **49**: 1947, 1949.
45. SHERMAN, R. S.: *Ann. Surg.*, **120**: 772, 1944.
46. *Idem*: *Ann. Surg.*, **130**: 218, 1949.
47. SLEVIN, J. G.: *Am. J. Surg.*, **75**: 469, 1948.
48. SMITH, F. L.: *J. A. M. A.*, **99**: 2008, 1932.
49. STALKER, L. K.: *Am. J. Surg.*, **75**: 688, 1948.
50. STEINER, C. A. AND PALMER, L. H.: *Ann. Surg.*, **127**: 362, 1948.
51. TAYLOR, K. P. A.: *Am. J. Surg.*, **45**: 145, 1939.
52. THEIS, F. V.: *Surg. Clin. North America*, p. 134, 1948.
53. WARREN, R., WHITE, E. A. AND BELCHER, C. D.: *Surgery*, **26**: 435, 1949.
54. WHITE, E. A. AND WARREN, R.: *Surgery*, **26**: 987, 1949.

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CASE REPORTS

CEREBROSPINAL FLUID RHINORRHŒA AND RECURRENT PURULENT MENINGITIS*

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Prior to about a decade ago recovery of patients suffering from purulent infections of the meninges, excepting meningococcal, was very rare. Since then, as a result of the use of the sulfonamides and the antibiotics in the therapy of these serious infections, the recovery rate has increased considerably. It has thus become possible for a person to have repeated attacks of purulent meningitis, and remain perfectly well in the intervals between them. Reports of a number of such instances[1 to 6] have been published in recent years, most of them being associated with head injury.

The following case report is of interest because the patient had an intermittent cerebrospinal fluid nasal drip and recovered from three separate and distinct episodes of acute purulent meningitis caused by different micro-organisms, and also because the abnormalities which were responsible for the existence of a communication between the subarachnoid space and the nose were disclosed and successfully treated by an exploratory operation.

A.S., a 10 year old boy, was first admitted to the Children's Memorial Hospital on June 12, 1948. The chief complaints were painful eyes, headache, vomiting and neck stiffness. The physical examination revealed an acutely ill child with extreme nuchal rigidity, generalized increased muscle tone, hyperactive reflexes and a positive Kernig's sign. The white blood count was 15,000 with a neutrophilia of 86%. The spinal fluid was turbid, and had a cell count of 1,620, of which 90% were polymorphonuclear cells. Spinal fluid, blood and throat cultures were positive for *H. influenzæ*, type B. The cerebrospinal fluid sugar was 14.4 mgm. %, the chlorides were 400 mgm. % and the protein was 112 mgm. %. The treatment consisted of sulfadiazine, streptomycin and *H. influenzæ* antiserum, type B. No intraspinal therapy was given. The patient made a good recovery and went home well on the 13th hospital day.

The second hospital admission was on November 7, 1949, almost 17 months after the first attack. He had had a mild cold for 2 to 3 days, and complained of a burning sensation over the right eye, vomited and be-

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came unconscious a few hours before his admission. He had been perfectly well since his recovery from the previous episode. Physical examination revealed nuchal rigidity and a positive Kernig's sign associated with a generalized convulsion. The pupils did not react to light. The blood leucocyte count was 7,300 with a differential of 1,606 neutrophils, 803 juveniles, 2,774 lymphocytes and 2,117 eosinophils. The spinal fluid was turbid and showed a 2 plus Pandy reaction and 1,625 leucocytes, all polymorphonuclears. On direct smear there were Gram-negative rods resembling *H. influenzæ*, but no growth was obtained on culture. The spinal fluid sugar was 101 mgm. %, the chlorides were 425 mgm. % and the protein was 177 mgm. %. There was a transient hæmaturia following intravenous sulfadiazine therapy. No further sulfadiazine was given, and he continued to receive penicillin and streptomycin which were administered from the inception of treatment. No intrathecal therapy was given. Roentgenologic examination of the paranasal sinuses showed no abnormality. The boy returned to his home in good health on the 17th hospital day.

On January 7, 1950, two months after the last admission, the patient was re-admitted in a semi-comatose state. He had had an intermittent watery nasal discharge since the previous admission. This attack began about three hours before he arrived at the hospital. He complained of pain over the right eye, vomited repeatedly and had twitching of the right side of the mouth. The child was semi-comatose and showed slight nuchal rigidity, with an extensor plantar response on the right side. The leucocyte count was 18,100 with a predominance of polymorphonuclears. The spinal fluid was turbid and under increased pressure. The Pandy test was 3 plus. The cell count revealed 990 leucocytes, of which 550 were neutrophils and 440 lymphocytes. Spinal fluid, blood and throat cultures all showed a heavy growth of *D. pneumoniæ*, type xii. The spinal fluid contained 115 mgm. % of sugar, 434 mgm. % of chlorides and 141 mgm. % of protein. The treatment consisted of penicillin and sulfadiazine. No intraspinal therapy was done. Recovery was rapid and complete.

In an attempt to find some explanation for the recurrence of purulent meningitis the history was carefully reviewed. In January 1947 the boy received a very minor laceration by a skate which just grazed the skin over the lateral part of his right eyebrow. Since his recovery from the second attack of meningitis there had been a thin watery right-sided nasal drip at times, especially when the head was inclined forward. This was also observed during convalescence in the hospital after his last illness. Drops from the right nostril yielded a specimen consisting of about 0.25 c.c. of clear fluid which grossly resembled spinal fluid. Roentgenologic examinations of the skull, chest and paranasal sinuses showed no abnormality.

In view of the strong possibility that a communication existed between the subarachnoid space and the nose, the patient was transferred to the Montreal Neurological Institute to the service of Dr. W. V. Cone for further investigation and treatment. Examination of the fluid from the nose showed it to contain 125 mgm. % of sugar and 1,020 mgm. % of chlorides. A blood Kahn test was negative. An electroencephalogram revealed an area of depression of the electrical activity over the right frontal region. Roentgenologic examination at this time showed some cloudiness of the sinuses on the right side. X-ray examination of the skull again showed no evidence of fracture or other abnormality.

On February 13, 1950, Dr. Cone performed an exploration of the anterior cranial fossa on the right side. The operative report was as follows: "An erosion of the dura through which the cerebrospinal fluid leak was undoubtedly occurring was found in the region of the right cribriform plate anteriorly over the roof of the right frontal sinus. There was an associated venous abnormality consisting of a large vein entering the origin of the sagittal sinus in this region. Fascial transplant from the temporal muscle was used to close the defect through an intradural approach. The venous anomaly was clipped. It is felt that the defect is probably related to the venous anomaly rather than direct trauma." The patient made an excellent recovery and has remained well with no further nasal discharge.

DISCUSSION

There have been numerous reports of relapsing meningitis, mostly meningococcal, in the literature, but true recurrent bouts of meningitis have been uncommon.

The prognosis in purulent meningitis other than meningococcal, which was previously almost uniformly fatal, has greatly changed since the advent of the sulfonamides and the antibiotics. Prior to this time recurrences were unlikely since the patient very rarely survived a first attack.

In neurosurgical clinics cases of recurrent meningitis in patients with spinal fluid leakage are now not rare. At the Montreal Neurological Institute Dr. W. V. Cone[7] has treated at least six, most of them secondary to trauma of the skull. Among them there was a child with hydrocephalus and an erosion of the skull at the site of the Pacchionian bodies, and a man with an osteoma at the base of the skull in which a dehiscence of bone had occurred.

Relapses occur within a relatively short interval after the initial attack and if a positive culture is obtained the organism is the same. There is often irreversible damage done due to chronic infection of the meninges with repeated flare-ups. Relapses may also result from a chronic focus of infection elsewhere in the body that has been resistant to therapy. Treatment is difficult and the results often poor.

On the other hand, recurrent meningitis refers to two or more separate and distinct attacks of meningitis usually occurring after a long interval of good health. Definite proof that the attack is a new infection rests on finding a different organism in spinal fluid culture.

The meninges may be infected by the hæmatogenous route from a focus elsewhere in the body. This may be recognized as pneumonia or a furuncle, or it may be slight and undiscovered as in the case of a mild upper respiratory infection. Possibly organisms may occasionally invade the blood stream through an apparently normal mucous membrane. Meningitis may also occur by direct extension from a primary focus, such as otitis or sinusitis. Less commonly, a defect in the dura leading to a pathway which allows pathogenic organisms from the nose or ear to enter the subarachnoid space may be responsible for the development of meningitis. This may follow a head injury or, more rarely, it may be due to

a congenital anomaly. It is important to realize that the injury may not be severe. In fact, it may be very slight and not show distinctly by careful roentgenologic examination, as in the case of a slight fracture of the lamina papyracea of the ethmoid. Furthermore, it should also be kept in mind that the injury may have been sustained many years previously. In a case reported by Hoyne and Schultz[1] the first attack of meningitis occurred eleven years after a head injury. The patient had five attacks of meningitis in five years, the last one ending fatally. At autopsy two small perforations behind the crista galli were found. These communicated with the ethmoid cells and the nasopharynx.

Practically all of the cases of recurrent meningitis reported in the recent literature give a history of previous head injury. Some, but by no means all, showed radiological evidence of skull fracture.

Recurrent meningitis in any patient, especially if there is a history of previous head injury, should suggest the possibility of a communicating track between the subarachnoid space and the nose or ear. It may require posturing to obtain spinal fluid from the nose or ear; in our patient the head was tilted forward. If a cerebrospinal fluid leak can be demonstrated from either of these apertures surgical exploration by a neurosurgeon offers the only hope of cure. Temporizing with daily administration of sulfonamides and antibiotics as a doubtful measure is a poor substitute. Despite the high incidence of cure with modern therapy, purulent meningitis is still a very serious disease, both from the standpoint of mortality as well as recovery with unfortunate sequelæ.

A case in which seven separate attacks of meningitis occurred in a child is reported by Schwartz and Champlin.[2] There was a head injury resulting in a skull fracture of the right frontal bone. There was a period of four months between the head injury and the first attack. A right frontal craniotomy was performed after the fifth attack. This revealed pachymeningitis involving the cribriform plate, but no fracture or nasal communication could be found. There were two subsequent attacks of meningitis following operation. Prophylactic sulfadiazine was then given intermittently and there were no recurrences in a four year period.

Traut[3] reported a case of a seven year old child who was admitted to hospital for five acute attacks of pneumococcic meningitis. An uncomplicated skull fracture had occurred two and one-half years before the first attack. The intervals between attacks were three to twelve months. X-ray examinations of the lungs, skull, and sinuses were negative. There was no investigation for a possible dural defect.

An interesting case of a man with a severe skull fracture and the initial attack of meningitis occurring thirteen years later was described by Libby.[4] The fracture was associated with bleeding from the ears, nose and mouth. After the first attack there were numerous recurrences or relapses, all bearing a relationship to the withdrawal of sulfonamides. No focus of infection could be found. There was no operation.

In 1940 Elvidge and Roseman[5] reported a case of pneumococcic meningitis with two recurrences. The initial attack developed two days after a severe head injury with a compound depressed fracture resulting in communication of the frontal-ethmoid sinuses with the nasal cavity. There was drainage of blood and cerebrospinal fluid from the wound.

Weinstein and Stanley[6] had a patient with nephrosis in whom a recurrence of meningococcal meningitis occurred 237 days after the initial attack. They discuss the differential features between a relapse and recurrence.

Congenital dermal sinus must be kept in mind in patients with repeated attacks of meningitis. This serves as a ready source of reinfection. Walker and Bucy[8] observed that the history in these was rather typical. In each case, there was found a dimple in the midline of the back at various levels. Evidence of meningeal infection generally appeared early in life. Waring and Pratt-Thomas[9] had under observation a patient with a congenital dermal sinus and four bouts of meningitis. The sinus was removed surgically, after which one more attack occurred.

Cerebrospinal fluid rhinorrhœa was stressed by Locke[10] as a condition which may occur in patients with brain tumour. He reported 14 fatal cases of cerebrospinal rhinorrhœa, all with brain tumour. Eleven cases had a communication connecting the floor of the anterior cranial fossa with the nasal cavity. One case showed a thinning of the floor in this region. There was proved meningitis in 10 cases with clinical signs in two. Two cases were discarded because of incomplete data. The excellent state of health of our patient in the intervals between his attacks of meningitis was good evidence against the possibility of a tumour of the brain.

SUMMARY

A case of recurrent meningitis with cerebrospinal fluid rhinorrhœa is presented in which three separate attacks occurred, caused by different organisms. There was a previous history of minor head injury. Operation after recovery from the last attack revealed a dural defect with an associated venous abnormality. It was felt that this latter condition was directly related to the dural defect. Following surgical treatment there has been no further nasal cerebrospinal fluid leak and the patient has remained well. Cases of recurrent purulent meningitis are not as rare as they were prior to the improved recovery rate of one or more attacks, as a result of therapy with sulfonamides and antibiotics. Indication for exploration and treatment by a neurosurgeon is emphasized.

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REFERENCES

1. HOYNE, A. L. AND SCHULTZ, A.: *Am. J. M. Sc.*, **214**: 673, 1947.
2. SCHWARTZ, N. H. AND CHAMPLIN, F. B.: *J. Pediat.*, **35**: 611, 1949.
3. TRAUT, E. F.: *J. A. M. A.*, **129**: 273, 1945.
4. LIBBY, D. H.: *J. A. M. A.*, **127**: 981, 1945.
5. ELVIDGE, A. R. AND ROSEMAN, E.: *Canad. M. A. J.*, **42**: 460, 1940.
6. WEINSTEIN, L. AND STANLEY, E. D.: *New England J. Med.*, **234**: 364, 1946.
7. Personal Communication.
8. WALKER, A. E. AND BUCY, P. C.: *Brain*, **57**: 401, 1934.
9. WARING, J. I. AND PRATT-THOMAS, H. R.: *J. Pediat.*, **27**: 79, 1945.
10. LOCKE, C. E. JR.: *Arch. Neurol & Psychiat.*, **15**: 309, 1926.

INTRAMEDULLARY SPINAL ABSCESS CO-INCIDENT WITH SPINAL ANÆSTHESIA*

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Although cerebral abscess[1] is a relatively common sequel of infections elsewhere in the body, abscess of the spinal cord is extremely rare. The lesion was first reported by Hart[2] in 1830. Arzt[3] in an excellent review of the literature was able to collect only 39 reported cases of intramedullary spinal abscess.

The reported cases appear to be about equally divided as to the source of the infection, half arising by direct contiguity from infection in the vertebræ and adjacent tissue, and half arising from far distant foci by way of the blood stream. As in cerebral abscess, infection in the chest is a common source from which a septic embolus finds its way to the cord.

The case reported here is intramedullary in type and secondary to a small pulmonary abscess.

This 76 year old male was well until five days before admission to hospital when he suffered a sudden severe pain over the lower three ribs in his right chest at the level of the anterior axillary line. The next morning he noticed frank hæmaturia in the absence of any burning, frequency or nocturia. He was admitted to hospital for a urological investigation.

On admission, a tense nervous old man was seen complaining of severe pain in th right upper quadrant of the abdomen and lower right chest. There was some impaired resonance and increased tactile fremitus with rough expiratory sounds at the right base posteriorly. The pulse was 60 and regular, the blood pressure 172/80, and the heart moderately enlarged to the left with the apex in the 5th space at the anterior axillary line. A low pitched blowing mitral systolic murmur of grade II intensity was heard.

Rectal examination revealed a smooth, moderately hypertrophied prostate and there was 11 ounces of residual urine.

A cystoscopic examination was carried out under spinal pontocaine anæsthesia and both ureters were catheterized. A retrograde pyelogram was taken and nothing abnormal was seen. In addition to this procedure, the patient was given a pentothal anæsthetic and an aortogram was carried out following the injection of 10 c.c. of 80% NaI solution into the abdominal aorta. This procedure clearly outlined the renal arteries and showed no evidence of tumour.

Following these operative procedures the patient developed a flaccid paralysis with complete associated sensory loss from the level of T. 2 downwards. The level of paralysis and sensory loss became fixed at T. 12 and remained there until the patient's death 21 days after admission, and 20 days after cystoscopy under spinal anæsthesia.

A single spinal puncture, done six days after the initial paralysis, revealed an initial pressure of 75 mm. of H_2O, on coughing this was raised to 150 mm. Nine c.c. of fluid was removed and the final pressure was 40 mm. The cerebrospinal fluid was clear, with a 4 plus Pandy, 4 white blood cells and 4 red blood cells per c.mm., and a colloidal gold curve of 1111112100.

The final neurological opinion was either spinal cord tumour or a post-pontocaine radicular lesion with severe flaccid paralysis of all myotomes below the level of T. 12.

The therapy carried out after this was purely palliative. The patient continued a gradual downhill course and died 21 days after admission.

AUTOPSY FINDINGS

There was a moderately hypertrophied prostate which microscopically showed a benign hyperplasia. Several of the periprostatic veins were thrombosed. The urinary bladder was hypertrophied, with the wall measuring 1 cm. in thickness and showing trabeculation. The mucosa of the bladder was shaggy and several petechiæ were seen on the surface. The microscopic picture was that of an acute and chronic cystitis, with muscular hypertrophy, foci of lymphocytes, plasma cells, and macrophages, and a diffuse infiltration of polymorphonuclear neutrophiles.

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Both ureters and kidney pelves were slightly dilated and in the right kidney pelvis the mucosa was roughened and discoloured purplish-red. A few c.c. of granular black material was seen in the right pelvis. The kidneys weighed 150 gm. each. The capsule stripped readily to reveal a coarsely granular cortical surface, with areas of purplish discoloration in the right kidney. On cross section, the cortico-medullary junction was prominent and again in the right kidney bands of pale discoloured tissue were seen radiating through the parenchyma from the pelvis to the cortex. On microscopic examination there was a pyelonephritis of both kidneys but it was much more acute in the right and showed some areas of microscopic abscess formation. Bacterial stains revealed clumps of Gram-negative bacilli in this necrotic debris. For the most part these organisms were short bacilli with rounded ends, but a good deal of pleomorphism was present, with coccoid and filamentous forms. The uninvolved cortical tissue showed moderate arteriosclerotic scarring with some tremendously dilated tubules and a few hyalinized glomeruli.

The pyelonephritis described above is felt to be due to urinary obstruction by an enlarged prostate with resultant cystitis and retrograde infection of the kidneys.

The lungs showed a patchy bronchopneumonic consolidation in the lower lobes. In addition a fresh infarct measuring 3 x 2 x 1 cm. was seen along the lateral diaphragmatic border of the right lung, and a small thrombus was demonstrated in the vessel supplying the area.

Near the periphery of the right upper lobe of the lung a small abscess cavity was seen measuring 3 cm. in its widest diameter. The cavity was filled with purulent exudate and the surrounding lung tissue was firm and indurated. Microscopically, clumps of Gram-negative bacilli morphologically similar to those seen in the kidney were demonstrated together with numerous Gram-positive organisms. There was no specific cellular reaction present, and the abscess cavity showed a good deal of fibrosis in the wall together with a heavy infiltration by both mononuclear and polymorphonuclear leukocytes.

The pleura over the abscess cavity and in the interlobar fissure was roughened and discoloured. A single old fibrous band extended from the apex of the lung to the overlying parietal pleura. The only finding at autopsy that might explain the patient's initial chest pain is the minimal amount of pleurisy overlying the abscess, since the infarction to the right lower lobe was more recent.

The brain showed no gross lesion.

Spinal cord.—A granular diffuse exudate was seen over its lower two-thirds. After several days fixation the cord was serially sectioned. It was found to be soft from the level of T. 3 downwards. In the upper thoracic region a central area of discoloration and softening 0.3 cm. in diameter was seen. This central area of softening extended from T. 1 downwards becoming broader until all the cord was softened by T. 3.

This central area microscopically was completely demyelinated and below T. 3 the entire cord was demyelinated and necrotic. The central vein contained a thrombus which showed early organization. The nerve and glial cells in the infarcted area showed marked degenerative change, but very little acute cellular infiltration was present, except on the meningeal surface where an exudate consisting principally of polymorphonuclear neutrophils was seen. Bacterial stains again demonstrated Gram-negative rods in the exudate and in some of the small blood vessels in the meninges.

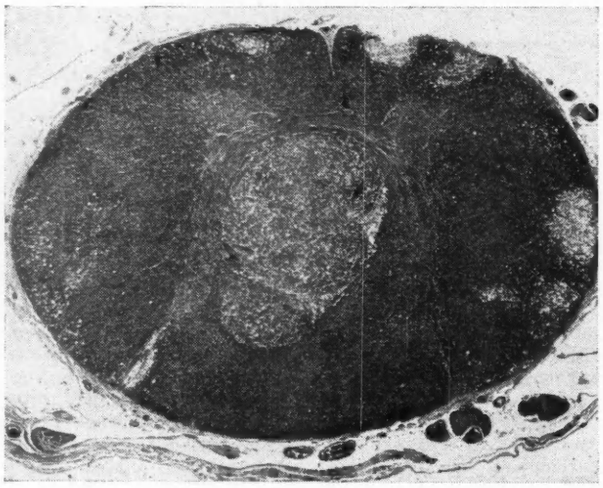

Fig. 1.—Transverse section of the cord at the level of T.1 stained for myelin showing a central area of infarction and demyelination.

It is felt that the sequence of events was as follows. The patient developed an acute sup-

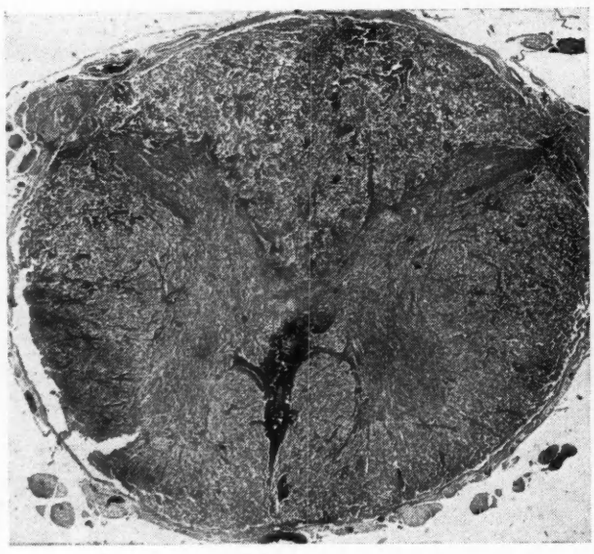

Fig. 2

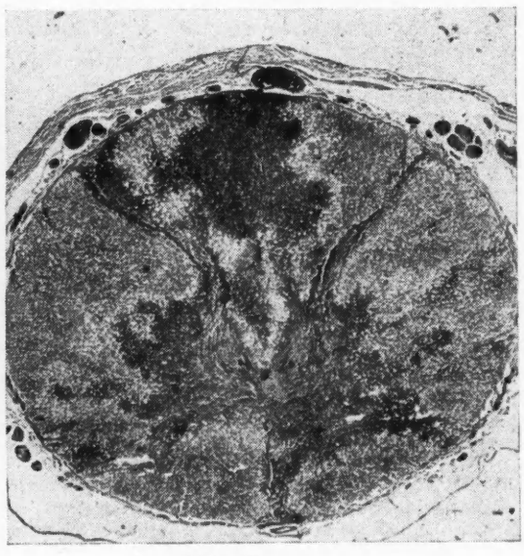

Fig. 3

Fig. 2.—Transverse section of the cord at the level of T.3 showing complete infarction, loss of myelin and a thrombus in the central vein. **Fig. 3.**—Transverse section of the cord at the level of T.12 showing large areas of demyelination.

purative pyelonephritis due to prostatic obstruction. A septic embolus gave rise to a pulmonary abscess which in turn was the source of a rare metastatic intra-spinal abscess. No evidence was found to lead us to believe that the spinal anæsthetic contributed to this cord lesion. There was no trauma resulting from the puncture for the aortogram.

We were greatly concerned about this case because it seemed highly probable the paralysis was the result of his spinal anæsthetic. In our department of urology we have an experience approaching 10,000 cases and have never had a similar catastrophe, although the recent literature is somewhat alarming. It must be admitted that there may be many minor residual effects of which we are unaware, but it is our experience that patients are quick to notice such untoward effects and that if they were common we would hear of them.

SUMMARY

A case of intramedullary abscess of the spinal cord is reported. This lesion was considered to be secondary to a pulmonary abscess which in turn arose from an acute pyelonephritis caused by retrograde infection due to prostatic obstruction. If a post mortem had not been obtained this would undoubtedly have been recorded as resulting from spinal anæsthesia.

REFERENCES

1. ANDERSON, W. A. D.: Pathology, 1st ed., Mosby, p. 1400, 1948.
2. HART, J.: *Dublin Hosp. Rep.*, **5**: 522, 1830.
3. ARZT, P. K.: *Arch. Neurol. & Psychiat.*, **51**: 533, 1944.

FAMILIAL HÆMOLYTIC ICTERUS OCCURRING DURING PREGNANCY

H. H. C. Johnson, M.D. and John E. McAllister, M.D.
Calgary, Alta.

Cases of hæmolytic icterus occurring during pregnancy have been recently reviewed by Bains and Doone[1] and by McElin.[2] In all cases where hæmolytic icterus occurred splenectomy was performed. McElin cites five cases. All were diagnosed prior to the sixth month. The outcome of the pregnancies were: three living infants, one stillborn, and one postmaturely which lived thirty minutes.

Mrs. G.R., a 34 year old white para 3 with a normal pelvis, Rh positive and negative Kahn had an expected date of confinement of June 10, 1950. Her history was marked by four episodes of severe jaundice dating to age 13. Congenital hæmolytic icterus had been diagnosed during 1938, and spenectomy had been refused. She had also had a cholecystectomy performed in 1938 for cholelithiasis.

Her obstetrical history consisted of: (1) a full term spontaneous delivery in 1936, resulting in a living normal infant; (2) a twin pregnancy during 1948, during which severe jaundice developed in the 29th week. A spontaneous premature labour followed, and the infants succumbed because of immaturity. The jaundice cleared spontaneously shortly after birth.

The present pregnancy also showed no remarkable finding until the 29th week. A moderate hypochromic anæmia (Hgb. 9.1 gm.) had shown a fair response to iron therapy. On March 29 right upper quadrant pain, vomiting, nausea, and jaundice appeared. There was right subcostal pain. The hæmoglobin was 9.8 gm. After a few days in hospital on parenteral fluids plus a fat-free carbohydrate diet, she was allowed to leave hospital on April 12, apparently free of symptoms. On April 17, following a two day recurrence of the above symptoms, she was readmitted to hospital. She now complained of severe weakness and marked flatulence, in addition to the above symptoms. Physical examination revealed a spleen which could be palpated half the distance to the iliac crest. There was also considerable icterus and marked tenderness in the right subcostal area.

Laboratory findings.—Hgb. 3.2 gm., red blood cells 1,260,000. The capillary fragility test showed hæmolysis beginning at 0.50% and complete at 0.31%. The reticulocyte count was 10.4%. The serum bilirubin was 3.10 mgm. (direct reaction 2.8 mgm. 10 minutes; 3.0 mgm. 30 minutes; indirect reaction 30 minutes 3.10 mgm.).

Treatment consisted primarily of replacement transfusion 1,000 c.c. of citrated blood being given daily until May 2. In addition parenteral glucose and amino acids were necessary for five days. Liver extract and vitamin B_{12} were given to favour erythropoiesis. On May 2, fourteen days after admission the acute hæmolytic process had cleared and the level of hæmoglobin had gradually increased to 12.8 gm. She was discharged from the hospital at this time.

A very slow drop in hæmoglobin followed, until admission in labour June 4, when the value was 10.2 gm. The labour was remarkable, an 8 lb. 1 oz. normal male being delivered spontaneously after a 2 hour 20 minute labour.

Splenectomy at this stage of the pregnancy would have presented considerable difficulty and in view of the favourable response to medical treatment was not considered necessary. Likewise the successful conclusion of the case justifies a decision against early termination of the pregnancy by induction of labour or Cæsarean section.

COMMENT

This case demonstrates an acute exacerbation of an hæmolytic icterus during the last trimester of pregnancy. A similar episode likely occurred at the same time during the preceding pregnancy. The treatment has been entirely conservative.

REFERENCES

1. BARNES, A. C. AND DOAN, C. A.: *Am. J. Obst. & Gynec.*, **55**: 864, 1948.
2. MCELIN, T. W., MUSSY, R. D. AND WALKER, C.: *Am. J. Obst. & Gynec.*, **59**: 1036, 1950.

SPECIAL ARTICLE

PARTNERSHIP OF THE STATE, THE MEDICAL PROFESSIONS AND THE COMMUNITY*

Sir Earle Page, G.C.M.G., C.H., F.R.A.C.S., F.R.C.S.(Hon.)

Australian Minister of Health, Canberra, Australia

The test of the efficiency of a national health scheme must be improvement of the health of the nation and the individual—the lessening of disease, progressive elimination of causes of disease, and a continuous rise in the qualitative excellence of medical practice. A scheme satisfying this test will come only from the active, continuous partnership of governments, the medical and allied professions and the individuals of the community. I hope to show that the judicious union of government aid with nationwide voluntary insurance against sickness and disease can create such a partnership between the government and the individual in which the traditional intimate doctor-patient relationship, that has been the glory and inspiration of medicine since the time of Hippocrates, can be maintained and developed with the minimum of governmental control or interference between doctor and patient.

This partnership is a recognition that the State, individuals and medical profession have obligations in a national health scheme. All will benefit: The individual will gain better health, longer life and an easier mind against the expense of sickness. The State will gain from more efficient production, from less manhour loss, and from greater national income and social stability. The doctors will benefit from a sense of security in their profession, from the opportunity of seeing their patients at an early stage and cutting down the duration of disease, with more time to study and absorb the medical experience gained from the treatment of each patient.

Such a partnership destroys nothing, but will make use of all those factors and organizations that have been built up over centuries to assist the restoration of health and prevent disease. This conception aims to keep everything that is good, and reject the obsolete. It will not destroy past advances in the medical art, but will make provision for the use of all future advanced methods through nationwide insurance against the cost of sickness and hospitalization. Our method of attack leaves everyone free to carry out the most effective handling of health problems—the doctor, the patient, the hospital management and staff, the chemist and the voluntary insurance organization. It keeps alive the element of initiative and competition in service that really produces progress.

Such an arrangement will leave the Government much freer to help in its own rôle of finance. Under the system proposed, the Government will have strict control over its own costs, leaving management of the insurance field to the voluntary societies. The patient and doctor both have a definite interest in preventing waste and abuse of time, skill, medicine and equipment, while the voluntary societies have a direct interest in preventing fraud.

In brief, our view is that a satisfactory health scheme can be satisfactorily operated only when there is complete co-operation and harmonious relationship between: (a) The providers of health services; that is, the hospital administrators and the medical, pharmaceutical and nursing professions. (b) The government, whose rôle should be concerned mainly with financial assistance, with perhaps some co-ordinating functions. (c) The community, who must be educated to partake of the services as they become necessary, and not to abuse any privileges.

The important group is, of course, the community, and it is well to bear in mind that no health service is satisfactory unless it extends to all sections of the community. If governments are to have a hand in assisting health services with financial aid it would be most unfair to exclude the wealthy who, after all, contribute largely to the revenue.

Voluntary prepaid insurance, backed by governmental aid, should be an attractive proposition to at least 85% of the people. Even those in the low income brackets should find no difficulty in meeting the low premiums—less than the price of a packet of cigarettes per week in some cases—which will provide the necessary coverage for their needs. I shall show that the remaining 15% can also be adequately cared for.

THE CHALLENGE TO THE MEDICAL PROFESSION

In the last analysis all medical care must be by individual doctor to individual patient. In actual fact, therefore, no real national health service can be provided without the willing and wholehearted co-operation and guidance of the doctors of the nation.

Here comes the challenge to the medical profession. Doctors are essentially self-dedicated and set apart to the service of their fellow men to save life and bring health. Their passionate devotion to these aims tends to make them become completely absorbed in the practice of their profession. But the time has come when, in the interests of the future existence and the future health of our race, and for the preservation of their own high and noble profession, doctors must take a special interest in the manner in which health problems are handled by the Government and the public.

* An address at the Academy of Medicine, Toronto, on August 14, 1951.

AUSTRALIAN HEALTH HISTORY

The last half century has seen in all countries a tremendous improvement in vital statistics, especially the reduction in the mortality rate and incidence of many diseases. This reduction has been due mainly to two factors—the remarkable discoveries of medical research into the causes of disease by various germs and methods of diagnoses, and the application of the discoveries to health problems on the advice of the medical profession.

I instance the improvement in health figures in my own country. Census figures show that the Australian infantile mortality rate per thousand per annum dropped from 118.40 in 1901 to 31.99 in 1947 and is still declining. At all ages up to 40 the rates of mortality in 1947 were approximately one-third of the corresponding rate of 1901 for males, and one-quarter for females. At the age of 60 the rate for males was 70% of the corresponding rate in 1901, whilst the female rate at 60 was only 60% of that of 1901.

Australian life tables—complete expectation of life—show that the expectation of life at the date of birth, according to the experience of the period, was in 1901 at 51 years for males and 54 for females. The census of 1947 showed that this expectation of life had risen to 66 years for males, and 70 for females. Taking the expectation of life at date of birth as a measure of the life efficiency of those born, it may be said that the experience of 1947 indicates a life efficiency about 29% in excess of that for 1901.

These results are an expression of the cumulative efforts of the medical profession on the whole health front during this period. Insistent advice and pressure of doctors in Australia, as in other countries, have ensured an improvement in water supplies, in sanitation and in immunization against infectious diseases. By the research of doctors, new germs, new drugs and new methods of treatment have been discovered. Doctors have learned by experience the effective use of these. The result is seen in this remarkable improvement in national health.

NECESSITY OF PROFESSIONAL CONTROL

But this remarkable advance may easily be lost overnight. The health of civilization is standing on the edge of a precipice if medical direction in the use of these discoveries is removed.

The experience of malaria in New Guinea in the last war is very illuminating in this respect. In the 20 years between the first and second world wars, remarkable improvements were made in the treatment and prevention of malaria. Yet, in the first six months of the New Guinea campaign against the Japanese, our soldiers, though under the strict governmental direction of Army control, suffered such disabilities from malaria, dysentery and scrub typhus as to reach the enormous annual proportion of 5,000 per 100,000 troops engaged; that is to say, 6 divisions would have been needed to keep 1 division in the field. This rate of disability was equalled only by the East African campaign in World War I when our armies were practically without medical supplies.

At the time this alarming position in New Guinea occurred there were available to the Army such expert malarial authorities as Sir Hamilton Fairley, Professor of Tropical Medicine of London University, and the most distinguished men from Harvard, Yale and Johns Hopkins, but the combatant commanders did not realize the vital importance of supreme medical control of this condition, At that time I was sitting in the Australian War Cabinet and raised the question of its rectification with the Australian Prime Minister. He requested Churchill and Roosevelt to insist upon medical discipline on approved lines and the full use of equipment and drugs available. Within a few months these measures reduced the disability rate from malaria to the lowest ever known in any war.

This incident gives a note of warning that these great advances of ours may go overnight. The ghastly health story of the internment camps in Europe and Asia show what can happen if full use is not made of medical achievements.

The point I wish to make is that while the health plan I outline leaves the proper functions of doctors completely free of governmental control, yet it is indispensable for its success that our best medical minds should disengage themselves long enough from their absorbing personal, professional work to ensure that health problems are wisely dealt with. Nationalization of medicine must be resisted at all costs. Mere transfer of a problem to governmental control does not solve that problem — it may even intensify it.

In any case, should not our free democratic people ask themselves why, when they have been able to obtain such magnificent results from our present health system, they should discard that system and attempt to sail on the uncharted sea of nationalized medicine?

In all medical nationalization schemes pressure to cover the whole field at once has led to chaos and those most needing care often do not receive priority. The better way, surely, is to move steadily upwards, step by step, building on the solid foundations of our past achievements and maintaining the great traditions of service and intimate doctor-patient relationship.

In our Australian national health scheme each of the partners, that is to say, the government, the medical and allied professions and the community, can take appropriate inter-related steps in their own rôle and sphere. The essence of this plan is to lessen the impact of sickness and, by the reduction of sickness, to lessen the consequent loss of productive capacity throughout the community. By means of a basic grant of governmental aid directed to prevent or shorten disease, it aims to stimulate throughout the whole community the spread of prepaid voluntary insurance schemes covering the greater part of

hospital and medical costs. This lessening of the cost of individual medical and hospital treatment will encourage the patient to seek early diagnosis and treatment and thus start the beneficial circle to reduce the total cost of treatment —both human and physical.

THE RÔLE OF GOVERNMENTS

The Government's rôle is to take such initiative in preventive measures as will secure community assistance and action.

Firstly, Federal and State governments can raise steadily the standard of medical treatment by the provision of ample numbers of highly-trained and experienced specialists, general medical practitioners, nurses, pharmacists and research students. This contribution would be by Federal and State governmental aid in the capital cost of building, and provision of modern equipment to universities, medical schools, and teaching, base, district and community hospitals. Combined with this, provision should be made for a home nursing service which is often cheaper and happier for the patient. Provision should also be made for the treatment of the aged and chronic in special wards in institutions instead of treatment in general hospital beds.

In this connection the Australian Government is lessening the entry into hospitals of the aged by providing free general medical practitioner service and free medicine to pensioners and their dependents, both in their homes and in the doctor's surgery. This is achieved by an arrangement with the Australian division of the British Medical Association on a concessional fee-for-service basis.

Secondly, the governments can take the initiative in improvement of sanitation by extending water supplies and sewerage installations. In the '30's the Australian Government carried these services into many small hamlets and towns by making an agreement to provide one-third of the interest and sinking fund costs on the condition that State governments and local communities each provided one-third. The effect of this measure on typhoid was seen in one town of about 15,000 people. There the annual recurrence of 700 cases of typhoid dropped to 2 or 3 which came from outside its area.

Thirdly, governments can improve nutrition and health by standardization of the quality and purity of food and drugs, with a definite lessening of sickness. The Australian Government has taken a further step in the improvement of nutrition by the free provision of milk to school children up to the age of 13 years in crêches, kindergartens and public and private primary schools. The milk is given the children during the morning recess and uniformly brightens up the youngsters for the succeeding lessons. The Education departments of the several States are actively co-operating in this program.

Fourthly, the Australian Government has made a direct attack on the killer diseases and on the incidence of infectious diseases by the free provision, on a doctor's prescription, of costly life-saving and disease-preventing and immunizing drugs to all sections of the community. Prevention of disease and curtailment of its duration by such means reduce the cost of hospital and medical care, both from the point of view of the government and the individual, lessen the country's loss from industry, increase total wealth production of the nation and pay for themselves several times over.

It is imperative that doctors should discipline this system of free drugs. In Australia the Federal Council of the British Medical Association has given the Government an advisory council of seven distinguished specialists and professors of pharmacology which decides what drugs should be free. The Council has also appointed a committee of four outstanding doctors to discipline doctors and chemists and prevent indiscriminate use of these powerful drugs. The result has been that in Australia the cost of this benefit has approximately equalled the original estimate.

Fifthly, my Government has taken a preventive measure by the provision of grants for medical research. The co-ordination of activities in this field has been brought about by the creation of a National Health and Medical Research Council which lays down the work to be done and prevents overlapping. The composition of this body consists of the Director-Generals of the Federal and State Health Departments, representatives from the medical faculties of universities and distinguished specialists.

The sixth preventive measure is the passage of laws making compulsory radiographic chest examinations in order to discover early tubercular infection, and the provision of liberal allowances to actual infectious tubercular cases and their dependents to enable such cases to rest sufficiently long with their minds at ease to arrest their disease and cease to be a danger to the public.

PARTNERSHIP OF GOVERNMENT AND VOLUNTARY INSURANCE

The preventive measures I have mentioned have been undertaken wholly by the Government because it is felt that the community benefit flowing from them may be as great or greater than the individual benefit. There now remains the field of medical and hospital benefits in which the individual gain is undoubtedly the greater. The Government's view is that this field should be covered by a system of prepaid voluntary insurance, operated by voluntary non-profit-making organizations experienced in that particular field. To encourage the develop-

ment of such organizations and to make the benefits attractive to their members, the Australian Government proposes to make available substantial grants-in-aid.

INSURANCE AGAINST MEDICAL COSTS

The present system of insurance against medical costs tends to be on a flat rate, to be limited by a definite income-earning capacity and to be confined almost exclusively to employed persons.

A wide extension of voluntary insurance to the community as a whole, and especially to the self-employed and rural elements in the community, can be secured by a basic grant of government aid towards extending the actuarial benefits possible under existing insurance schemes. Insurance would thereby be made so attractive as to induce many people to seek insurance cover without great expenditure on enrolling agencies. This grant-in-aid would be given only if participating insurance organizations at least matched the government grant for each item of medical treatment.

The grant, plus an equivalent amount of insured benefit, would meet approximately 80 to 90% of the fees charged to the lower income groups. Higher income groups would insure themselves for greater benefits, rendered more valuable by the existence of the governmental grant. There would be no direct connection between the government and the medical profession. Agreements would be made on a long-term basis with organizations providing insurance cover.

SPECIAL FEATURE OF THE AUSTRALIAN PLAN

I should now like to elaborate on a feature of our plan which is somewhat unique; that is, the proposal to make available to the patient, through his organization, the appropriate amount of governmental subsidy, even where the organization is precluded from paying a benefit under its own rules.

In a number of circumstances an organization, because of actuarial considerations, does not pay a benefit to its members. For instance, there is the usual condition that a member must go through a probationary or waiting period, usually two months in ordinary cases, and nine or ten months in confinement cases. Most organizations have a maximum amount which can be drawn on their funds during a calendar year. Then again, organizations will not usually pay a benefit for treatment of certain chronic disease, or for treatment of a complaint the symptoms of which were in evidence at the time of joining. We propose to make the governmental subsidy available to members of organizations in all these cases. Thus a man may become a member on his way to the doctor and be eligible for the grant.

Our view is that this will have a twofold effect: Firstly, voluntary insurance will be made very attractive. The man who would not ordinarily be bothered to join an organization will see the advantages, and once he becomes a member we think he will continue membership. Secondly, some portion of his medical expenses will be met by the government, and thus he will be relieved of the expense to that extent. From a financial point of view, the grant may often exceed his yearly contribution. We also think that the governmental grant will enable the organizations to liberalize their exclusion conditions.

In order to cope with the "in and out" person, that is, the man who pays one or two contributions to an organization to obtain the governmental grant and then drops out, we propose to follow the practice of the organization. If a member is in arrears with his premium, but is still regarded as being financial by the organization, the governmental subsidy will follow along with the organization's benefit. However, where the member becomes unfinancial under the organization's rules, and the organization refuses to pay a benefit until the arrears are paid, the governmental subsidy will also be withheld. Of course, an unfinancial member who pays his arrears will immediately be eligible for the governmental subsidy.

"Unable" section of the community.—A question sometimes asked is how is it intended to cover those people unable to join the voluntary prepaid insurance organizations? These may be divided roughly into two groups: Those who are financially able to contribute as members of organizations, but have been unacceptable for membership in the past because of age or for health reasons, and those who are acceptable for membership but have not sufficient finance to maintain membership.

Regarding the first group, the organizations have already indicated a readiness to liberalize their rules in the matter of age limits, and rarely refuse membership on the grounds of ill health. They may, of course, make the membership conditional, but it has already been explained that the governmental subsidy will flow to the patient in these cases.

The second group, that is, the indigent class, presents more difficulties, but in Australia the great majority of these are already provided for under the Pensioner's Medical Service which takes care of age, invalid and other pensioners and their dependants. It is estimated that not more than about 5% of the population will consist of indigents who are not already covered, and consideration is now being given to ways and means of reaching these people. It is thought that the solution will be either by way of subsidy through the organizations or direct screening and subsidy by the Government.

INSURANCE AGAINST HOSPITAL COSTS

The principle of prepaid voluntary insurance, similar to that proposed for medical expenses, is

being applied in Australia in regard to hospital costs. The several preventive measures I have already outlined, by lessening the incidence of sickness, will improve the position of hospital finances generally and the accommodation position. A still further improvement is being brought about by encouraging domiciliary treatment of minor illnesses. I have mentioned in passing the domiciliary treatment of pensioners and their dependents which is achieved by an arrangement with the Australian division of the British Medical Association, under which this group receives free treatment and free medicines, and the doctor is remunerated by the Government on a concessional fee-for-service basis.

When hospitalization is inevitable, however, we are meeting the position by an extension of the prepaid insurance principle. By joining a voluntary non-profit-making organization which handles hospital insurance, a person or any of his dependents will become entitled to a governmental grant of 12/- (twelve shillings) per day towards the costs of hospitalization. As there is a requirement that the voluntary organization must provide at least six shillings per day, a minimum of eighteen shillings per day is available to meet the hospital costs. In actual practice the total insurance is something more than that sum.

As in the case of medical benefits we believe that abuse is best avoided by leaving some portion of the hospital costs to be paid by the patient. Further, as in the medical benefits plan, the governmental daily grant will be available to insured persons in circumstances where actuarial considerations preclude the organizations from paying benefits from their own funds; for instance, during waiting periods, or where the maximum period under the organization's rules has expired, and for specific diseases not recognized by the organization.

SUMMARY

In summing up we think:

1. That emphasis should be placed on the preventive side of medicine. This is particularly important in a country where there are shortages of hospitals, hospital staffs and hospital equipment.
2. A health service should extend to all sections of the community. Therefore governmental grants-in-aid should be available to all the people.
3. In order to avoid abuse, and thus allow financial aid and medical services to be used to the fullest extent in genuine cases, the patient should meet a small part of actual expenses when they are incurred.
4. A successful health service requires complete co-operation between governments, the providers of the service and the people.

We are convinced a health scheme which satisfies all of these fundamentals will operate more smoothly than one which antagonizes certain sections, and which leaves a large body of the community without adequate cover against the risks of sickness and disease.

THE PROBLEM OF REFUGEE DOCTORS

[*In February, 1950 we referred to the grave problem which refugee physicians present to the licensing body of Ontario; the difficulties of language, and of investigating credentials are very great. The most recent report of the College of Physicians and Surgeons of Ontario contains the following further statement which shows the continuous effort which is being made in Ontario to deal with this problem.*—EDITOR.]

"The continued unsettled economic and political condition in many parts of the world is responsible for an increasing number of applicants for Enabling Certificates, and Council has requested that a second report be prepared giving the profession and the public an outline of the method of investigation followed before these applicants are granted an Enabling Certificate which allows them to write on the Examinations of the Medical Council of Canada.

"The committee fully realizes the importance of granting Enabling Certificates only to those fully qualified, always having in mind its responsibility in protecting the public from any who may not be thoroughly trained and fully competent to provide medical care to patients who entrust their health and lives to them.

"These unfortunate physicians are first of all interviewed by the College staff before they are permitted to make application for an Enabling Certificate. Every assistance is given them to secure preferably a rotating internship or, failing that, a position in a laboratory or as a ward attendant.

"From the fact that there are not enough desirable vacancies for them, many are temporarily employed in menial work until they learn the English language and become more or less acquainted with our Canadian way of life. There may be a waiting period of several months before they could get a position that would be helpful in their medical training. However, none of those whose qualifications fulfil our minimum requirements are ever refused making application for an Enabling Certificate.

"Results of examinations must be coupled with an evaluation of the quality of training, therefore each applicant for an Enabling Certificate is required to not only serve as a rotating intern for one year, but he must also make a personal appearance before the committee when his various certificates, diplomas, etc. are carefully evaluated. The Committee must also have

TABLE I.

REPORT DEALING WITH ALIEN PHYSICIANS GRANTED ENABLING CERTIFICATES 1946-1950 INCLUSIVE

Total enabling certificates granted		120
Total certificates issued	113	
Total certificates not yet issued	7	
	120	
Of the 113 certificates claimed—		
Number of applicants taking M.C.C. exams	73	
Number of applicants not having written	40	
	113	
Of the 73 candidates who have written the M.C.C. exams—		
Total number who have passed		51
First try	32	
Second try	12	
Third try	6	
Fourth try	1	
	51	
Total number who have failed		15
First try	6	
Second try	8	
Third try	0	
Fourth try	1	
	15	
Total number rejected completely		7
		73
First try	4	
Second try	3	
	7	

satisfactory confidential reports from the chiefs of staff of the hospitals in which he served his internship. The applicant must also present a satisfactory Curriculum Vitæ, and proof of application for Canadian citizenship.

"Important as is the standing of the school from which the physician graduated, the evaluation of his personal fitness is equally important.

"We know that many European medical schools of high repute suffered very severely in efficiency, and very little reliable information is available as to the present standing of the mid-European medical colleges.

"The applicants who present themselves before the committee are quite co-operative in assisting the committee to fairly evaluate his or her qualifications."

ERRATUM

Dans notre numéro de septembre, à l'article du Dr J. H. Palmer sur le Traitement de l'Angine de Poitrine, à propos du trinitrate de triéthanolamine, notre traducteur écrit qu'il "ne provoque que très peu d'effets secondaires", alors que l'auteur dit que c'est une particularité remarquable de cette drogue de *n'en pas* provoquer.

HOSPITAL REPORTS

ROYAL VICTORIA HOSPITAL COMBINED STAFF ROUNDS

No. 4

DIZZINESS—A Symposium

E. A. Stuart, M.D., W. J. McNally, M.D., Karl Stern, M.D. and G. M. Shy, M.D.

E. A. Stuart, M.D.

When asked to open this symposium on dizziness it was decided that I should present a number of illustrative cases taken from a series of 200 cases of dizziness, reviewed recently by Drs. McNally, McKercher, Lockhart and myself. The various aspects of the subject will be considered by the men who follow me. Illustrative case records are as follows.

True Ménière's syndrome or hydrops of the right labyrinth. A female, aged 49, in January, 1946 developed daily sudden attacks of rotatory dizziness with nausea for two weeks. Less frequent attacks followed. She had marked loss of hearing in her right ear, and had developed right-sided tinnitus at the time of her dizziness. The caloric tests showed a hypo-active right labyrinth. The cardiovascular system was normal. Her thyroid had been removed in 1938. Her basal metabolic rate in 1947 was minus 14. Six months after the onset of her dizziness she was given intravenous histamine over a period of two months with relief. In July, 1946 she had a hysterectomy. From November, 1946 to February, 1947 she received subcutaneous injections of histamine without relief. In July, 1947 the right labyrinth was destroyed by the ablation method of Cawthorne by Dr. McNally with complete relief of her dizziness. This patient complained of headache and had been exposed to considerable mental strain for a period of three years prior to the onset of her dizziness. It is doubted that the mental strain had anything to do with her attacks as she continued to be exposed to the causes of her mental strain after her operation.

Toxic labyrinthitis. — A male, aged 59, had sudden attacks of rotatory dizziness for a period of ten years before he was investigated. His attacks occurred on rising, lasted two to three minutes and recurred about once a month. He had loss of hearing, more marked in the right ear; he developed tinnitus in the right ear five years after the onset of his dizzy attacks. His caloric tests were normal. In 1943 he had an

electrocardiogram which showed evidence of coronary disease. His central nervous system was normal. He had a diseased gall bladder. In 1940 his symptoms responded favourably to thiamine chloride, but in 1942 failed to benefit from the same treatment. In 1943 he received injections of histamine for seven months without relief. In January, 1944 an eighth nerve section was advised, but not done. In June of the same year his gall bladder was removed and his dizziness ceased. Although this patient had evidence of cardiovascular disease, the dramatic relief of symptoms following the removal of his gall bladder suggested that if this is not a long remission infection in the gall bladder was an important factor in producing his symptoms.

Hypertension. — Twenty-five cases occurred in this series. A young lady of 36 developed sudden attacks of dizziness in 1947. The attacks lasted for about ten minutes, and recurrences were frequent. Two years prior to the onset of dizziness she developed bilateral tinnitus and headache, with a blood pressure averaging 180/100. She had no hearing loss. Her caloric tests showed bilateral hypo-active labyrinths. In June, 1947 she had a supra-diaphragmatic ganglionectomy with evulsion of T-12 and L-1 roots by Dr. William Cone. The blood pressure average was reduced to 140/90. Following this operation her dizziness and headaches disappeared; the tinnitus persisted. The dramatic relief which followed her sympathectomy strongly suggests that hypertension was responsible for her symptoms.

Coronary thrombosis. — There were 13 cases in this series. A male of 57 was first examined in 1938. In April of that year he was confined to bed for several days with sudden severe attacks of rotatory dizziness with nausea and vomiting. The dizziness continued for eight weeks. He had no loss of hearing. He had no tinnitus. He had a markedly hypo-active labyrinth on the right side. His blood pressure was 170 systolic. His central nervous system was normal. Seven years later, during a period of considerable mental strain, he died suddenly of coronary thrombosis, without ever having had a recurrence of the dizziness.

Cardiovascular disease in which the blood pressure fluctuated from 90 to 170 systolic. A male, aged 68, was examined for the first time in 1940. In 1937 he developed attacks of dizziness which occurred about once a week, lasting two to three hours. Nausea and vomiting were associated. Deafness increased during his attacks and left-sided headache preceded his attacks by a few minutes. Tinnitus in the left ear developed two years later than the dizziness. His caloric tests were normal. He had arteriosclerosis and a fluctuating blood pressure. In 1940 his central nervous system was normal. His dizziness subsided with very little treatment and from 1940 to 1948 he was free from dizziness. In 1948 he died of cerebral hæmorrhage. Although headache occurred in 50% of the cases in this series, in only 10% was there a definite association with the dizzy attacks. This was one of those cases, the attacks being ushered in by a headache of a particular pattern.

Atypical Ménière's syndrome. — Typical in most respects, this was considered atypical because of an occasional loss of consciousness during an attack. In every instance where loss of consciousness occurred in this series of cases serious disease in the central nervous system was eventually found. A female of 51 was first examined in April, 1943. In 1942 she developed attacks of dizziness of short duration, consisting of a swaying sensation. With the attacks she had headache and occasionally loss of consciousness. She had suffered from loss of hearing, and in 1941 had developed tinnitus in the right ear. Her attacks did not respond to adequate treatment with modified salt free diet, histamine and thiamine chloride. In 1948 she was found to have complete loss of hearing in her right ear and a loss of labyrinthine response in the same ear. An eighth nerve tumour was diagnosed and removed with cessation of headache and dizziness.

Psychosomatic disease. — A female, aged 22, was first examined in April, 1944, two months after the onset of attacks of dizziness. The attacks were described as a feeling of things rushing around in her head. She had no loss of hearing and no tinnitus. Frontal headache was associated with her attacks. The caloric tests were normal, and did not reproduce her spontaneous attacks. She was mildly depressed. The basal metabolic rate was minus 27. She did not respond to thyroid extract. In October, 1944 she was given electric shock therapy. Following this there was no further depression or dizziness.

This last group was characterized by a multiplicity of abnormalities such as fatigue, mental depression, thyroid deficiency and hypotension, all of which may be factors in the cause.

W. J. McNally, M.D.

We are using the word dizziness here to mean a consciousness of disorder in the postural mechanism. Posture depends upon the vestibular, the ocular, and the kinæsthetic systems. The perversion of the impulses from any one of these systems to the central nervous system leads to confusion and dizziness. With this conception one must, of necessity, survey a wide field in order to find the pathological process. We are most concerned with the vestibular mechanism and its part in the causation of dizziness.

Deafness and dizziness are frequently associated, and prior to Ménière's time it was well recognized that the deafness was the result of a lesion in the cochlea. Ménière was the first to suggest that dizziness might be due to disease in the near-by labyrinth. He described his now famous case, and the syndrome or the triad of

dizziness, deafness and tinnitus has been called Ménière's syndrome.

It remained for Hallpike and Cairns to show the histological changes in two cases of Ménière's syndrome which could be interpreted as hydrops of the labyrinth. There was evidence of increased pressure within the internal ear mechanism that caused dilatation of the cochlear duct, and some dilatation within the membranous labyrinth. It has not been generally conceded that the above findings comprise the whole of the pathological process in Ménière's syndrome, but a number of subsequent observers have confirmed the findings of Hallpike and Cairns.

My remarks today will concern the diagnosis, the assessment of the results, and the treatment which we followed in this series of cases. There is a widespread belief that a history of a sudden attack of rotary dizziness is necessary before one can make a diagnosis of Ménière's syndrome. It has been stated in the literature that such a sudden attack might be considered as diagnostic. We would say that a sudden attack of rotary dizziness is suggestive, but it is not diagnostic of a true Ménière's syndrome. A few years ago Dr. Stuart and I carried out a series of vestibular tests on relatively normal individuals. The sensations which they described following the direct stimulation of the labyrinth by cold water were as follows: the patient feels that he is going to faint; he feels unsteady; he has a rocking or a staggering sensation; he has a swimming sensation; a sensation of backward swaying or a waving sensation. This suggests that a patient suffering from labyrinth disease might well complain of any one of the above sensations.

The presence or absence of the symptom triad. The symptom triad is dizziness, deafness, and tinnitus. Its presence suggests a case of true Ménière's syndrome, but it may be found in a case of eighth nerve tumour or in a patient suffering from cardiovascular disease. If one of the members of the triad is deficient the case is often spoken of as one of atypical Ménière's syndrome. The disease may progress and the third symptom develop, but many of these atypical cases remain so, and are probably the result of extra-labyrinthine disease, such as a cerebro-vascular disturbance.

Tinnitus was present in about three-quarters of the cases in this series. In about one-quarter of the cases there was a history of some change in the tinnitus during the attack.

Headache was present in about three-quarters of the cases, but it appeared to be related to the attack in only about one-eighth of the cases. A history of a loss of consciousness during the attack invariably proved to be the result of organic disease in the central nervous system.

In 45% of the cases in this series there was evidence of extra-labyrinthine disease which was thought to be the cause of the symptoms. There was evidence of cardiovascular disease in 67 cases, and in 47 we thought it to be the cause of the symptoms. There were 35 cases in which there was central nervous system disease, and in 27 it was thought to account for the symptoms. It cannot be over-stressed that in a large number of these cases complaining of dizziness there was definite evidence of organic disease in the cardiovascular or central nervous systems capable of producing the symptoms.

Assessment of the results of treatment.—Many of these patients were observed over a ten year period or more. Long remissions from symptoms were frequently noted. Some of the longest remissions occurred in patients who were not receiving treatment. Fifty patients in this series had had no treatment, but they had remissions from symptoms, the average length of which was four years. It was decided that before any case could be considered as cured the period of freedom from symptoms must exceed the length of time of the average remission, and it was therefore suggested that five years would be the minimum period of freedom from symptoms which could be called a "cure". If the relief lasted for six months or more it was called a "temporary relief". If the symptoms recurred after a five year period the case was classed as one of "temporary relief". If the relief was less than six months it was spoken of as "symptomatic relief". There were 57 cases under investigation for five years before 1944. Of these there were 9 which could be considered to be cured. Of the 9, 7 had had no treatment. The same 57 cases were reviewed again at the end of 1949. Five were still symptom free and considered to be cured, and of the 5, 3 had had no treatment.

MEDICAL TREATMENT

1. *Restriction of sodium intake.*—Very few cases in this series followed a strict sodium free diet. In most instances the patient was put on a modified salt free diet with the administration of potassium chloride. It proved to be very difficult in each individual case to find out to what extent the recommended treatment had been followed. Furthermore in many cases different treatments were combined, and it is not easy to assess the effects of the various remedies. There were 67 cases receiving what was considered to be an adequate modified salt free diet with potassium chloride, and of these 5 were cured. In this group there were 31 cases of true Ménière's syndrome, of which 2 were cured and 8 had temporary relief. There were 28 cases in which we thought the treatment was inadequate and 4 were cured.

2. *Histamine.*—There were 20 patients treated with subcutaneous injections of histamine, and one-half of these patients obtained relief. There were 10 cases of true Ménière's syndrome in this group, 1 of which was cured, and 2 of which obtained temporary relief.

3. *Nicotinic acid.*—Thirty-four patients were treated with nicotinic acid, and three-quarters obtained relief. Of this group 15 cases were cases of true Ménière's syndrome. Six had temporary relief. The nicotinic acid was given in doses of 400 to 600 mgm. a day. It appeared to be the drug of choice, particularly in relieving acute attacks of dizziness.

SURGICAL TREATMENT

1. *Eighth nerve section.*—There were 9 cases in which one-eighth nerve was sectioned. Four of these obtained complete relief and were considered to be cured.

2. *Labyrinthine ablation.*—There were 5 cases in which one labyrinth was ablated. All these cases were within the last 5 years so that none could be considered a cure. Four of the cases were classed as temporary relief.

If the hearing in both ears is lowered the operation of choice is a differential section of the vestibular portion of the eighth nerve. This is done with a view to maintaining the residual hearing in each ear. If the disease is confined to one ear and if the hearing is normal in the opposite ear the simpler procedure is a labyrinthine ablation. The tinnitus may persist in spite of the operative procedure followed. Dandy reported that in his series of 400 cases, which included partial nerve section or total nerve section on one or both sides, the tinnitus persisted in 50% of the cases.

Surgery should be advised only after careful study has excluded organic disease from the cardiovascular and the central nervous systems, and after a thorough trial has been made of medical treatment.

Karl Stern, M.D.

Dizziness is one of the most frequent complaints encountered in psychiatric practice. However, when one inquires more carefully it happens quite often that the patient is not referring to true dizziness. Real vertigo occurs in people who have hypertensive cardiovascular disease together with, or on the basis of, a psychoneurotic maladjustment. Apart from that there is a large number of patients who, when they speak of dizziness, are talking either of a vague, ill-defined sensation of anxiety or something like astasia or abasia. The patient very often complains that he feels as if he had to hold on to something, otherwise he might fall. This is a symptom of anxiety. In order to evaluate the symptom choice, that is to say why patients will choose this particular type of symptom, we have to consider what determines symptom choice in general. The most productive approach from this point of view has been the psychoanalytical one. Careful psychoanalytical studies have shown that the symptom choice is determined through infantile experiences and conflict situations occurring in certain infantile stages, even if a symptom first appears at a certain age. For example, it can be shown that those patients whose symptoms manifest themselves mainly in the upper parts of the gastrointestinal tract, for instance in peptic ulcer, are patients in whom the root of the conflict lies in the so-called first oral stage, that is to say the phase in which the child is chiefly a passive recipient of maternal love. Patients whose symptomatology is mainly referable to the lower intestinal tract, such as mucous colitis, etc., are patients whose conflict is rooted in a phase somewhat later, around the end of the second year or in the third year of life.

As far as the complaint of dizziness is concerned there are, in my opinion, two elements which have to be taken into account. Firstly, on the basis of the cases I have seen I should say that those patients in whom dizziness is in the centre of complaint are people who encountered conflict particularly during the phase which corresponds to the development of upright standing and of walking. This is at the same time at the phase when the child in its relationship to the surrounding is facing his own aggressiveness, and the rivalry of others. Dr. Boulanger, Mrs. Cleghorn and I have lately published a study in which we investigated idiomatic expressions referring to body functions and emotions. From this point of view it is interesting that when we speak of such things as standing, walking, etc., we often refer to the social functions of aggressiveness, of success and failure, etc. We say, for example, about a person that he "cannot stand up for himself" or "he has to step out on his own for the first time now". We also say incidentally about someone that he is "dizzy with success" or that "his success went to his head". In all the cases in which the patient complains of dizziness as a prominent complaint I have found that the mechanism of his neurosis is a very marked situation of rivalry.

The second element we have to keep in mind is the general observation, clinical as well as from animal experiments, that emotions which are not discharged by the skeletal muscular apparatus (such as impulses to fight) have a tendency to express themselves in the vasomotor apparatus. This again leads us to the assumption that the sensation of dizziness has something to do with a repressed aggressiveness, either consciously withheld or unconsciously subdued.

In discussing the symptom of abnormal fear of heights I have pointed out before (in a different connection) that in my experience abnormal fear of heights is associated with a very ambivalent attitude towards success. If a man is approaching success in life and if his career leads him far "above" others he may develop a marked fear of heights in a true literal, spatial sense, and this depends on one question,

that is whether in terms of his infantile archaic phantasies his success is a strong act of aggression against a rival. In those people in whom dizziness is a prominent complaint there exists not infrequently a similar situation. I remember one particular case of a patient who came to see me for a few years at long intervals. He complained of dizziness in two situations. First when he was dealing with big-shots in his type of work, and second whenever he was inside Windsor Station, particularly when he was using the elevator. This was a man of 29 years of age, who came from a somewhat low social and economic environment, and who had had a rocketlike career. At this comparatively young age he held a high position in the insurance business. There was, as one could easily see on the basis of dream-analysis and free thought association, an extremely violent rivalry position with his father and with his younger brother. He became "dizzy with success" in a literal sense of the word. The fact that he had this sensation mainly when facing big-shots was easily explained. Windsor Station had the meaning to him of the weak little boy from the country (his parents lived in a small town outside Montreal and he commuted) stepping out into the big world. It is interesting to see that this man, by gaining insight into the mechanism and by being able to detach himself from the infantile layer, so to speak, became free of his symptom.

G. M. Shy, M.D.

We certainly agree with Dr. McNally that the term "dizziness" as we meet it is a vague one. The patient who complains of "dizziness" in the Neurological clinic often has a transient disturbance of consciousness, or vertigo or presyncope. The latter can be due to postural hypotension. Only about one-third of the patients that we see, who say they are dizzy, actually suffer from true vertigo. By vertigo, we mean that the patient is having some disorientation of his sense of position in space. This may be rotatory or simply a sensation of up and down movement.

There are three primary systems involved in the production of vertigo and these are the peripheral proprioceptive sensations, the eye-muscles and the vestibulo-cerebellar connections. The most important in our discussion here today are the vestibular connections.

The eighth nerve originates from the Scarpa's ganglion and from the labyrinth and semicircular canals and then goes to the superior portion of the medulla oblongata at the level of the superior part of the inferior olive; there it goes around the restiform body and impinges at least the vestibular portion, upon the vestibular nuclei. The stimuli are then referred out through the inferior cerebellar peduncle or the restiform body to the cerebellum. Robert Dow, in Oregon, has shown that almost all of these stimuli in the vestibular system are referred to the floccular-nodular lobe of the cerebellum. The fibres then come back by way of the same peduncle to the vestibular nuclei, hence the floccular nodular lobe is in itself almost a ganglion. Working on Dr. Dow's hypothesis, Bard removed this lobe in seasickness experiments performed during the last war. He found that dogs which previously became seasick did not become so after this portion was removed.

I will point out the neurological lesions that can be the cause of true vertigo. Dr. McNally has covered the ear quite well, such as toxic labyrinthitis, labyrinthian irritation, Ménière's syndrome, etc. The eighth nerve is a common site for neurological lesions and most common are the eighth nerve tumours, *viz.*, the perineural fibroblastomas and the bilateral eighth nerve tumours of the Schwann cells as seen in von Recklinghausen's disease.

As one approaches the cerebellar-pontine angle, cerebellar tumours pushing down on the nerve itself may cause vertigo, also meningiomas, cholesteatomas or other such tumours in this angle. In the brain stem at this level probably the most common disturbance is due to disseminated sclerosis. It is not unusual at all for a plaque to be found in one of these sites. Disseminated sclerosis is frequently initiated by vertigo and this may often be the first or most prominent symptom. Another lesion at this level is of the posterior inferior cerebellar artery which as you know supplies this area. This is not an uncommon syndrome.

More recently, since we have been treating both meningeal and pulmonary tuberculosis with streptomycin, our patients have been bothered by vertigo a great deal. It is known that streptomycin injures the vestibular nuclei almost exclusively and people on prolonged streptomycin therapy, may lose entirely their vestibular responses. The other possible cause of vertigo from this level is a tumour in the fourth ventricle, the so-called ependymoma which pushes down against the vestibular nuclei.

Cerebellar disturbances give vertigo in two ways, one of course by the pressure on the floccular-nodular lobe and the other by pressure against the 8th nerve itself as it goes across the cerebellar-pontine angle.

In the central nervous system, the occurrence of arterial sclerotic episodes in the brain, thrombosis, hæmorrhage, sudden increase of intracranial pressure may cause vertigo. It is uncommon however for repetitive vertigo to be present unless the lesion lies within the vestibular system. Similarly, extra-ocular muscle paresis can cause subjective vertigo.

There is one other neurological entity which we would like to point out and that is what Gowers called "vertiginous epilepsy". More recently most observers think that this falls into temporal lobe. Anatomically the connections be-

tween the vestibular nuclei and the temporal have not been well demonstrated but it has been well shown, I think, that focal lesions in the temporal lobe may be preceded by a vertiginous aura. The other group includes patients whose seizures begin with adversive head movements which give a false sense of vertigo.

The therapy which we use is essentially that described by Dr. McNally. Occasionally we have had good results in people with eighth nerve tumours awaiting operation with dramamine. The only other thing that I would like to point out is that, when the vertigo is severe as with thrombosis of the posterior inferior cerebellar artery and when the patient is nauseated and vomiting, correction of fluid balance becomes the primary treatment before other definitive measures may be carried out.

CLINICAL and LABORATORY NOTES

FLAME SPECTROPHOTOMETRY
II. Sodium and Potassium in Blood and Urine

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The basic physiological and clinical disturbances that cause electrolyte imbalances have been recognized for many years. These include conditions such as anorexia, diarrhœa, vomiting, acidosis, renal abnormalities, etc. In recent years a great deal of new information has become available on the subject of electrolyte balance in man. This has been made possible largely by the development of the flame photometer which, in turn, has given us a quick and accurate method for the determination of sodium and potassium. Thus we can now recognize and evaluate the imbalance that is at times produced by replacing the loss of only one electrolyte, sodium chloride. This imbalanced replacement can aggravate the deficiency of the other electrolytes after long periods of poor intake or excessive loss.

In the first paper of this series an outline was given for establishing optimum characteristics for quantitative flame spectrophotometry applicable to any metallic ion. In this paper we detail the procedures established for estimating the sodium and potassium content of blood and urine. These have now been utilized most satisfactorily during the past four months.

STANDARDS

(A) *Stock solutions*

NaCl: 1.0166 gm./100 c.c. (contains 400 mgm. % Na).
KCl: 0.2861 gm./100 c.c. (contains 150 mgm. % K).
$(NH_4)_2HPO_4$: 0.341 gm./100 c.c. (contains 80.0 mgm. % P).

(B) *Working solutions*

NaCl: Dilute the stock solution 10:100 (the Na "S" stock).
KCl: Dilute the stock solution 2:100 (the K "S" stock).
$(NH_4)_2HPO_4$: Dilute the stock solution 5:100.
$CaCO_3$ 27.4 mgm./100 c.c. The carbonate is dissolved by adding an equivalent amount of hydrochloric acid before diluting the solution to the mark.
$MgCl_2.6H_2O$: 70.1 mgm./100 c.c.
Urea: 2.0 gm./100 c.c.

(C) *Working standards*

(a) *Sodium standards* (for serum and urine).

To each of a series of seven 100 c.c. volumetric flasks, numbered (a) to (g), add the following:
0.4 c.c.—$MgCl_2$ solution.
0.8 c.c.—$CaCO_3$ solution.
1.0 c.c.—$(NH_4)_2HPO_4$ solution.
6.5 c.c.—K "S" stock.

Add to each flask in turn the following amounts of Na "S" stock in c.c.'s, then dilute with water to the mark:

a	*b*	*c*	*d*	*e*	*f*	*g*
7.40	7.70	7.90	8.10	8.30	8.50	8.70

These solutions represent, respectively, the following concentrations of Na in terms of mgm. %: 296, 308, 316, 324, 332, 340 and 348.

(b) *Potassium standards* (for serum)

Because there is interference with the K estimation by the Na present, three series of standards are made—A, B and C—each consisting of ten 50 c.c. vol. flasks. Add to each of the flasks the following:
0.4 c.c.—$MgCl_2$ solution.
0.8 c.c.—$CaCO_3$ solution.
1.0 c.c.—$(NH_4)_2HPO_4$ solution.

A series (for samples containing approx. 340 mgm. % Na).

To each of the flasks add 8.50 c.c. Na "S" stock. Then, in sequence, add the following quantities of K "S" stock (in c.c.) and dilute to the mark with water:

a	*b*	*c*	*d*	*e*	*f*	*g*	*h*	*i*	*j*
4.00	4.30	4.80	5.10	5.80	6.20	6.50	6.80	7.20	7.50

These dilutions represent, respectively, the following concentrations of K in mgm. %: 12.0, 12.9, 14.4, 15.3, 17.4, 18.6, 19.5, 20.4, 21.6 and 22.5.

B series (for samples containing approx. 324 mgm. % Na).

To each flask add 8.10 c.c. Na "S" stock. Then follow with the K "S" stock solution as in series A.

C series (for samples containing approx. 308 mgm. % Na).

To each flask add 7.70 c.c. Na "S" stock. Then follow with the K "S" stock solution as in series A.

(c) *Potassium standards* (for urine).

Two series of standards are made—Au and Bu—each consisting of seven 50 c.c. vol. flasks. Add to each of the flasks the following:
0.1 c.c.—$MgCl_2$ solution.
0.07 c.c.—$CaCO_3$ solution.
1.0 c.c.—$(NH_4)_2HPO_4$ conc. stock solution.
1.0 c.c.—urea solution.

Au series (for samples containing more than 260 mgm. % Na).

To each flask add 0.88 c.c. Na "S" stock. Then, in sequence, add the following c.c.'s of K "S" stock and dilute to the mark with water:

a	*b*	*c*	*d*	*e*	*f*	*g*
3.0	4.0	5.0	6.0	7.0	8.0	9.0

These dilutions represent, respectively, the following concentrations of K in mgm. %: 90, 120, 150, 180, 210, 240 and 270.

Bu series (for samples containing less than 260 mgm. % Na).

To each flask add 0.44 c.c. Na "S" stock. Then follow with K "S" stock as in series Au.

N.B.—All sodium and potassium stock solutions should be measured from a burette.

PROCEDURE

The Sample.

(a) Serum is diluted—1:50 for potassium estimation; 1:100 for sodium estimation. If cloudy, the serum must be centrifuged and, if necessary, also filtered.

(b) Urine is diluted—0.1:50 for potassium; 1:100 for sodium estimation. These dilutions are approximate since variations in urine concentrations are considerable. Therefore, preliminary readings must be taken and correct dilutions deduced from the initial results.

If the urine is turbid, it should be well mixed, an aliquot removed and gently heated until all crystals are dissolved.

(c) Other liquids can be analyzed in a similar manner. However, if the composition is markedly different from that of serum, special standards must be made approximating the composition of the unknown.

The Instrument.

(a) The power charger is brought as close as possible to 0 amperes. If the more common trickle charger is used it must be completely disconnected from the battery when the spectrophotometer is in use.

The instrument is allowed to warm up for about 20 minutes in the check position, shutter closed. The dark current is centred. The water is turned on and the heating chamber plugged in.

(b) The instrument settings for analyses are as follows:

	Sodium	*Potassium*
Wavelength	592.2	774
Slit	0.12	0.38
Sensitivity	4 turns from counter-clockwise	4 turns from clockwise
Gas (propane)	1½ cm.	2 cm.
Oxygen	29	20
Air	25	23

The exact position of the wavelength dial should be determined for each instrument as it may vary slightly.

Working Procedure.

(a) Whenever the instrument is to be used for flame work, the cuvette carrier should be removed from its chamber.

(b) Sodium readings are always taken first, since the amount of sodium in the sample will later determine which of the three series of potassium standards should be used for the potassium analysis.

(c) The samples to be analyzed are poured into small 5 c.c. beakers which are protected from dust particles. This can be done conveniently by arranging them in a cigar-box from which the front wall has been removed.

(d) Preliminary readings of the unknowns are taken in order to determine which standards are suitable for comparison.

(e) In order to start the flame, all controls on the panel should be closed. All tanks should also be closed.

Open the gas tank. Flush out the gas line by opening gas control briefly and letting some gas escape. Then open the gas control very slightly and light the burner. Adjust the gas flow to the desired pressure on the manometer.

Open the oxygen tank and adjust the pressure on the panel. Adjust the water flow until the water is hot, but not boiling.

(f) Turn selector switch to 0.1 and adjust dark current. Then place a beaker of distilled water under the atomizer and turn on the air to the correct pressure.

Check the dark current again, then open shutter and centre the galvanometer with the transmission dial. This reading represents the flame-background. It should read about 0.5 for sodium, 1.0 for potassium.

Close the shutter at the end of the reading. Turn off the air before removing the beaker. (This prevents the atomizer from being clogged by dust from the air.)

Take readings of unknowns in the same way, flushing out atomizing chamber between readings with water.

Select suitable standards (three for each unknown) and read them together with the unknown. Then plot the standards on graph paper and read the unknown concentration.

NOTE:

(g) Be sure to check the oxygen pressure, air pressure and dark current constantly, as they tend to drift. Sodium readings especially are very critical as the normal range 315 to 345 mgm. % is represented by a transmission range of only 3 or 4%!

If, during a reading, the galvanometer drifts markedly to the right, either (a) the atomizer is blocked or (b) the rubber diaphragm is wet. If the diaphragm is wet it will stick tightly to the rim of the beaker and a vacuum is formed which reduces the rate of atomization. In this case remove the beaker and dry the diaphragm.

If the atomizer is blocked, remove it from the chamber, place the tip in a beaker of water and turn on the air to about 10 to 15 lb. Place your thumb over the outlet and allow the air to go in reverse *i.e.*, through the tip). This will dislodge clogging particles.

When shutting off the instrument turn off the oxygen tank first. When oxygen pressure has fallen to zero, shut off the gas. This procedure prevents a back-fire while disengaging the instrument.

SUMMARY

An outline is given in some detail for the quick and accurate determination of sodium and potassium in blood and urine. This procedure is directly applicable to the DU Beckman spectrophotometer with a standard flame attachment utilizing propane, oxygen and air pressures. However, with slight modifications it is equally applicable to other types of instruments.

THE ELECTROCARDIOGRAM AND DISTURBANCE OF POTASSIUM METABOLISM.—The authors point out that potassium is primarily an intracellular ion and exerts its major physiologic effects within the cell. Electrocardiographic changes reflect these intracellular effects and cannot necessarily be correlated with serum potassium levels, with which they are frequently at variance. Case reports are presented to indicate correlation between the clinical condition, electrocardiographic changes and intracellular potassium deficiency.—Currens, J. H. and Crawford, J. D.: *New England J. Med.*, **243**: 843, 1950.

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EDITORIAL

THE PROGRAM FOR THE ANNUAL MEETING

THE preparation of the program for our annual meetings is an extremely arduous affair. Until some years ago it was customary for it to be drawn up by a committee at the locale of the meeting. But as the Association has grown, this method has proved to be unsatisfactory. In the building up of a program for a national group it is most desirable that, so far as possible, it should be handled by those who are experienced in the work. This means the formation of a committee which will be more or less permanent; at any rate, one whose personnel will not change every year.

Such a committee has been formed and has been in operation for many years. It is known as the Central Program Committee. As it is essential that the General Secretary should be in the closest possible touch with the committee and serve as its secretary, the committee is located in Toronto, and its members are all drawn from Toronto, representing as far as possible all the various branches of Medicine. Furthermore, the frequent meetings (which are held every week, for a month or two) make it impracticable for attendance by out of town members.

Now, while this committee has the task of correlating the various elements of the program, provision is made for a definite share in the work by the local program committee which is always set up in each place of meeting by the Division responsible in that year. This local committee sends in suggestions to the central committee which fits them into the program so far as is possible. The central committee alone has the complete records and experience which enable it to select a program balanced both as to type of material and representation from all Divisions.

Work begins on the program early in the fall of the preceding ear. The Central Program Committee's first step is to obtain from the local divisional committee its general suggestions as to speakers and the type of program. From then on it is constantly engaged in collecting material and in deciding what should be used. All members of the Association have the right to submit or suggest contributions, but obviously there must be selection within the not too wide limits of the program.

It is equally obvious that the committee must have early notification of suggestions. Frequently, requests to contribute to the program are received too late to be considered. In general, the committee should have the names of all potential contributors no later than the end of the year, since the invitations to speakers are issued at about that time.

If any member has a paper which he would like to present at the next meeting, to be held in Banff in June, 1952, the General Secretary should be so advised, not later than December 1, 1951.

Editorial Comment

R. SAMUEL McLAUGHLIN FOUNDATION

We note with pleasure the establishment of a foundation created by R. S. McLaughlin of Oshawa. This will provide assistance to Canadian medical school graduates, selected for staff appointments by their own or some other Canadian medical school, to enable them to visit and study at medical centres in foreign countries or in Canada. Financial support will also be given to promising medical research in Canada.

It is Mr. McLaughlin's hope that the foundation will help to counteract the exodus of brilliant young Canadian doctors by providing fellowships on a scale hitherto unknown in this country. The idea for this foundation was conceived by Dr. W. Edward Gallie of Toronto. The foundation is endowed with an amount in excess of $1,000,000.

The Fourteenth Annual Louis Gross Memorial Lecture will be delivered at the Jewish General Hospital in Montreal, under the auspices of the Montreal Clinical Society, on Wednesday, October 17, 1951, at 8.30 p.m., by Dr. Myron Prinzmetal, Associate Professor of Medicine, University of California, Los Angeles; His subject will be "The Auricular Arrhythmias".

MEN and BOOKS

THE CONCEPT OF LEVELS OF CONSCIOUSNESS IN THE UPANISHADS*

(A Historical Note)

Edward L. Margetts, M.D.

Allan Memorial Institute of Psychiatry, McGill University, Montreal, Que.

It is clear from the Sanscrit writings that ancient Indian philosophers had a pretty good idea of what we nowadays call "the unconscious". One of the earliest works to indicate this is the Upanishads, a collection of documents, dating about 600 B.C., which constituted the earliest written presentation of the efforts of the Hindus to construe the world as a rational whole, and to regard the ultimate as a unification of the individual self with the Supreme Being, the Absolute, Brahma.

Sanscrit scholars have written in great detail about the "types of soul", or levels of consciousness, in the Upanishads.[3 to 6] The German philosopher, Arthur Schopenhauer (1788-1860), was greatly influenced by them. Alcorn[1] believes that Paul Carus[2] derived his theory of the unconscious from the Upanishads, since Carus was a student of Indian philosophy.

The Upanishads, particularly Mandukya Upanishad 3-11 (ref. 7 pp. 391-3), set forth quite clearly the "four states of self". They are:

1. The waking state (*jagarita-sthana*). Equivalent to the "Conscious". Man accepts the universe as he finds it. Perception, volition, and memory are preserved. This state is recognizable in the well-developed animal kingdom, including man. (According to Vedanta philosophy, a psyche exists in animal, vegetable and mineral kingdoms).

2. The dreaming state (*svapna-sthana*). The "Subconscious". The self loses contact with reality, and the soul fashions its own world in the imagery of its dreams. The usual state of mind in the less developed animal kingdom.

3. The deep-sleep state (*susupta-sthana*). A deeper level of the subconscious approaching complete unconsciousness. State of bliss in which there is no contact with reality, no desire, no dreams. This is the situation in the vegetable and mineral kingdoms.

4. The fourth state (*caturtha, turiya, turya*). The "Super- (or Supra-) conscious". "According to Vedanta, it is in this state that Seers get flashes of Great Truths in the form of vague apprehensions, which are afterwards elaborated in the jagrat state or waking consciousness".[8] Deussen[4] reasoned that full appreciation of this state of soul became prominent with the rise of the Yoga school, which believes that by intense meditation and self-control, the union of the human soul with the Supreme Soul, Brahma, may be achieved, *with the maintenance of the waking consciousness.*

* *This historical investigation was supported by a grant from the Ciba Co., Ltd., Montreal.*

REFERENCES

1. ALCORN, D. E.: Sigmund Freud and Psychoanalysis, *Bull. Vancouver M. A.*, **16**: 204, 1940.
2. CARUS, P.: The Soul of Man. Open Court, Chicago, 1891.
3. DASGUPTA, S.: A History of Indian Philosophy, 4 vols., University Press, Cambridge, 1922-1949.
4. DEUSSEN, P.: (a) The Philosophy of the Upanishads. Translated by A. S. Geden, T. & T. Clark, Edinburgh, 1906. (b) The System of the Vedânta (etc.). Translated by C. Johnston, Open Court, Chicago, 1912.
5. GARBE, R.: Vedanta, J. Hastings, Encyclopædia of Religion and Ethics, T. & T. Clark, Edinburgh, 13 Vols., Vol. 12, p. 597, 1908-1926.
6. GEDEN, A. S.: Upanisads, Hastings, Vol. 12, p. 540.
7. HUME, R. E.: The Thirteen Principal Upanishads, 2nd ed., rev. by G. C. O. Haas, Oxford University Press, London, 1931.
8. RAVI VARMA, L. A.: (I am indebted to Dr. Ravi Varma of Trivandrum, S. India, and I here quote from one of his letters to me.)

NOTE.—Accents have been omitted from the Sanscrit words in the text.

MEDICAL SOCIETIES

Canadian Dermatological Association

At the Annual Meeting of the Canadian Dermatological Association, in Montebello, Quebec, June 18 and 19, 1951, there was an attendance of fifty-three members and guests. The presiding officer was Dr. E. Gaumond. Sixteen papers were presented. In addition to these, a clinical meeting was held at the Hotel Dieu Hospital on June 20.

The following officers were elected: President—Dr. B. Usher, Montreal, Que; Vice-President—Dr. J. P. Foisy, Montreal, Que.; Secretary Treasurer—Dr. S. E. Grimes, Ottawa, Ont.

Canadian Association of Pathologists

The third Annual Meeting of the Canadian Association of Pathologists was held at the Pathological Institute, McGill University, on June 19, 1951. The subjects discussed included: "The Training of Laboratory Technicians", "The Standardization and Accuracy of Laboratory Tests", "Laboratory Services for Civil Defence", and "The Economic Status of the Pathologist". It was also decided that the Association should operate a registry of pathologists and a registry of positions vacant in order that those pathologists seeking a position would have knowledge of possible posts. This registry will be operated by the Secretary-Treasurer of the Association, Dr. M. B. Mackenzie, Herbert Reddy Memorial Hospital, Westmount, Mtl. 6, Que.

The following slate of officers was elected for the ensuing year: President, D. F. Moore, St. Paul's Hospital, Saskatoon; Eastern Vice-President, M. O. Klotz, Ottawa Civic Hospital, Ottawa; Western Vice-President, Daniel Nicholson, Department Pathology, University Manitoba, Winnipeg; Secretary-Treasurer, M. B. Mackenzie, Herbert Reddy Memorial Hospital, Tupper St., Montreal.

REGIONAL REPRESENTATIVES

British Columbia—Wm. Boyd, Banting Institute, 100 College St., Toronto.
Alberta—John Duffin, Colonel Belcher Hospital, Calgary.
Saskatchewan—Dean W. S. Lindsay, University of Saskatchewan, Saskatoon.
Manitoba—J. M. Lederman, Medical College, University Manitoba, Winnipeg.
Ontario—W. L. Robinson, Banting Institute, 100 College St., Toronto; W. J. Deadman, Hamilton General Hospital, Hamilton; D. Magner, Department of Pathology, University of Ottawa, Ottawa.
Quebec—G. L. Duff, 3775 University St., Montreal; L. C. Simard, Institut d'Anatomie Pathologique, Université de Montréal, Montreal.
New Brunswick—Arnold Branch, Lancaster Hospital, Saint John.
Nova Scotia—O. C. MacIntosh, St. Martha's Hospital, Antigonish.
Prince Edward Island—J. H. Shaw, Laboratories, Department of Health and Welfare, Charlottetown.
Newfoundland—J. E. Josephson, St. John's General Hospital, St. John's.

Ontario Medical Association District Meetings

The Lakehead Summer School in conjunction with the annual meeting of District Ten was held at Fort William and Port Arthur on September 6, 7 and 8. Dr. K. J. R. Wightman, Toronto, spoke on "The Use and Abuse of Antibiotics" and on "ACTH and Cortisone in Hæmatological Disorders" and gave two medical clinics. Dr. J. Allan Walters, Toronto, spoke on "Psychotherapy, the Healing Art of Every Physician" and on "Pain and Suffering"; "Diagnosis and Therapy". He held two neuropsychiatry clinics. Dr. F. A. B. Sheppard, Winnipeg, gave two papers on surgical topics and held two surgical clinics. A ladies' dinner was held at the Port Arthur Golf and Country Club under the chairmanship of Mrs. F. F. P. Thompson while her husband chaired the dinner at Prince Arthur Hotel for the doctors.

District Nine held a meeting at North Bay September 9, 10 and 11. Toronto speakers were Dr. Wallace Graham on "Recent Advances in the Treatment of Arthritis"; Dr. Keith Welsh on "Management of Gastro-intestinal Hæmorrhage"; Dr. John Mann on "Some Practical Points in the Application of Obstetrical Forceps"; Dr. Harry Botterell on "Recent Advances in Neurological Surgery"; Dr. A. W. Farmer on "Surgery of the Hand". Dr. H. S. Little of London spoke on "Some Intestinal Conditions in Infancy". A dinner followed by a dance, attended by the doctors and their wives was held at the Empire Hotel. LILLIAN A. CHASE

There is a great force active in the world, poisoning men's minds, that may put culture and science back, as they were put back once before, for a long period. It is a matter for very serious thought that when these revolutionary ideas infiltrate great communities, the first action of the leaders when they achieve a coup d'état, is to attack those who have been trained in scientific methods, those who are accustomed to independent thought and are not easy victims of mass propaganda.—Lord Alfred Webb-Johnson.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

GENERAL PRACTITIONERS' REMUNERATION

The request of the British Medical Association for the submission to arbitration of the whole question of remuneration of general practitioners, referred to in this correspondence last month, has been acceded to by the Minister of Health, with one proviso. This proviso represents a matter of emphasis rather than of principle. Whilst the B.M.A., not unnaturally, lays prime emphasis upon the total amount available for such remuneration, the Minister regards it as of "the first importance . . . that a new plan should be devised for the distribution of the pool (*i.e.*, the money available for the payment of general practitioners' fees). The Minister therefore proposes (1) the immediate establishment of a working party, composed of representatives of the General Medical Services Committee (of the B.M.A.) and of the departments concerned to make out a redistribution of distribution; (2) to seek a decision by an independent adjudicator of the sum (payable per patient) which should be used in calculating the size of the central pool."

The B.M.A. has agreed to accept whatever decision may be reached following arbitration, but it adds "the profession would feel rightly aggrieved if the award following arbitration were nullified by failure to agree in the working party upon a proper distribution of the pool". In view of the history of the negotiations between the Ministry and the B.M.A. since 1948, this is not an unwarranted fear on the part of the latter, but if both sides are sincere in their desire to provide the best possible service for the public, there should be relatively little difficulty in agreeing on a suitable scheme.

THE GERIATRIC PROBLEM

One of the major problems under the National Health Service is the increasing extent to which the hospitals of the country are filling up with the elderly sick. What happens is that an elderly patient is admitted to hospital for some condition such as pneumonia or a fracture. Once he or she is fit for discharge, it is found that there is no place to which the patient can be sent, as the relatives are often unable or unwilling to care for him after leaving hospital. Then there is the other type of elderly or aged patient who no longer requires the skilled supervision found in hospital but is not fit to be discharged home as a certain amount of nursing is still required. For such a patient to remain indefinitely in a general hospital merely means an increasing delay in the admission of younger patients requiring active treatment.

The same thing is occurring in the mental hospitals, and in their recently published report for 1950 the Board of Control point out that patients over 65 represent an increasing proportion of the total admissions and of the patients resident in hospital. This increase is out of all proportion to the increasing percentage of old people in the population. The problem is a mixed socio-medical one, and though much has been talked about it, relatively little has been done by the authorities. On the other hand, voluntary organizations such as the Nuffield Foundation have done as much to alleviate the problem as they could within their financial means. It is not a problem, however, which under modern conditions can be solved by voluntary means. The Ministry of Health must accept full responsibility.

TREATMENT OF CHRONIC RHEUMATISM

A year ago a committee was appointed by the Royal College of Physicians of London to consider the organization of the treatment of the chronic rheumatic diseases. In their report, which has now been published, the committee consider that the chronic rheumatic diseases should not generally be a whole-time specialty, but should constitute a special interest within general medicine. For the diagnosis and treatment of these diseases

an adequate background of general medicine is essential, and in addition some special knowledge of orthopædics, physical medicine and endocrinology is necessary. They recommend that special centres should be set up throughout the country, preferably one in each hospital region (of which there are 14 in England and Wales and 5 in Scotland). These centres would be primarily concerned with research and teaching, but would also influence the general standard of teaching. They would be linked with the medical department of a general hospital and university teaching and research departments. The centres would be in the charge of a physician with good general medical experience and special training, and the minimum period of training for such a physician would be six years after the completion of his house appointments. There will be general agreement with the insistence of the committe upon the necessity for the physician in charge of such centres being primarily a good general physician, and general relief that the committee has decided against the establishment of a special diploma in the subject.

R.A.M.C.

This is not the usual place to review books, but there will be many Canadian doctors who served with the Forces during the 1939-45 war who will wish to obtain and read a recently published short history of the Royal Army Medical Corps (''Not Least In The Crusade'', by Peter Lovegrove). Although written primarily as the official textbook for the instruction of junior officers in the history of the Corps, it deserves a much wider public. It provides a fascinating history of the medical services of the British Army since the days of the Romans, and illustrates well the official obstruction and obscurantism against which the leaders of the Corps had to struggle, even up to quite recent times. Written in a clear attrative style it will appeal to all medical men who saw active service during the last two world wars. It is also a fitting tribute to the memory of the 2,463 members of the Corps who laid down their lives during the 1939-45 war. Copies (price 5s. each in England) can be obtained on application to The Editor, *Army Medical Services Magazine*, Queen Elizabeth Barracks, Crookham, Hants. London, September, 1951. WILLIAM A. R. THOMSON

OBITUARIES

Dr. Cecil C. Birchard of Montreal, died on July 30 of a dissecting aneurysm of the right common iliac artery. He had been in a severe motor accident some months before, from which he had never quite recovered. He was born November 19, 1886, at Valentia, Mariposa Township, near Lindsay, Ont. After preliminary studies, he entered Lindsay Collegiate Institute. He then proceeded to the University of Toronto where he graduated with honours in medicine in 1911. He joined the Sun Life Assurance Co. in August, 1915, and was appointed chief medical officer for the company in November, 1916. He retained that position until his death. One month after his appointment as chief medical officer he went overseas and served until 1919 with the Canadian Army Medical Corps.

After his pioneer work in Montreal in electrocardiography, Dr. Birchard was named attending physician and director of the Department of Clinical Electrocardiography at Montreal General Hospital. He retired from its active staff in 1950, and also from the position of associate professor of medicine at McGill University.

When the Canadian Medical Association, at its annual meeting in Winnipeg in 1947, organized the Canadian Heart Association, the pioneer work of Dr. Birchard was recognized and he was named president of the Association. At his death he was still a councillor.

In company with Dr. I. M. Rabinowitch in 1937, Dr. Birchard went on board the *S.S. Nascopie* to the Arctic regions for a two-year study of Eskimo diseases.

Earlier this year Dr. Birchard had been elected vice-president of the Montreal Medico-Chirurgical Society. He was also president of the Canadian Life Insurance Medical Directors Association, a member of the University Lodge, and active in the Masonic Order. He is survived by his widow and two sons.

AN APPRECIATION

Not many men had as diverse interests as Cecil Birchard, or ''Birch'', as he was always known to his friends; nor the mental power to pursue them so vigorously. And even if he had no particular knowledge on a given subject he could always put difficult questions about it. Probably, as time went on, some of his juniors gained more detailed knowledge of cardiography than he. But his philosophic approach to it always placed him above them. Cardiography was peculiarly suited to his genius. As a house surgeon in the Montreal General Hospital in 1914 he quite naturally took to himself the care of the first electrocardiograph in Montreal. It was then an instrument unapprehended by the average physician, or indeed even by the heads of the medical services of the hospital, but to Birch's '' 'satiable curtiosity'' and mechanical ingenuity it soon yielded up its mysteries, and from the very beginning it was obvious that he would be the leader in a department whose methods were to become so essential in diagnosis. The translation of the cardiogram—always within its acknowledged limitations—is now in essentials easily within the capacity of all clinicians, but in the early days when the tracings still had their esoteric quality, ''Birch'' was one of the few who had the gift of clearly describing how they were produced.

He probably was the first, in Canada at any rate, to show by means of his then ponderous machine, and while still a house surgeon, that the heart might continue to beat for a time even if there was clinically acknowledged death.

But versatility and restless activity were only part of his unusual personality. He took his ideas from no one but rather delighted in developing a point of view different to the conventional; and if it were diametrically opposed he defended it all the more vigorously. To hear him in argument with his friend ''Rab'' (Dr. I. M. Rabinowitch) when they were bachelor companions, was to know what heights of dialectic could be reached short of invective. But it was not all for talk's sake alone. ''Birch'' had an extremely shrewd and practical mind, and one would often find that what had seemed at first to be an extravagant claim, was not to be so lightly dismissed, certainly not while he defended it.

Unconventional he always was, but if in consultation on a case he would spread the various cardiographs on the floor and then stretch himself at full length on the carpet to study them, it was all done in a perfectly natural way. He might then proceed to talk at great length to the patient about anything rather than his illness, but later it would be found that Birch had left with him a deep impression of genuine interest in his welfare. He was never above details and would often himself do what others might leave to the house surgeon or nurse. If a case in the public ward interested him particularly he would spend time on it without thought of other engagements. Indeed he had a faculty of making himself difficult to find.

No one could ever accuse him of being sentimental, but he was unfailingly genial, and his most trenchant criticisms would be delivered with a humour that roused no rancour. He was steadily loyal to his hospital, his friends, and his ideal of truth. H.E.M.

Dr. Arthur Oswald Brown, aged 69, a Vancouver physician died on July 17 in his Crescent Beach home where he retired five years ago. Dr. Brown took his medical degree in Western University, London, Ont., and later did graduate work in Rochester and Los Angeles in eye, ear, nose and throat. He practised in Alberta before coming to Vancouver 24 years ago. He leaves his widow and one daughter.

Dr. Urgel Gariepy, prominent French-speaking surgeon, died in his 70th year at Prefontaine, Quebec, on August 17. Retired from active practice since 1948,

Dr. Gariepy was a Fellow of the American College of Surgeons and of the Royal College of Physicians and Surgeons of Canada. In addition he had been a member of the Academie Médicale de Paris and of the Canadian Medical Association. He was a former president of La Société de Chirurgie de Montréal and professor at the faculty of medicine of the University of Montreal.

During World War I, he was a member of the Canadian Army medical staff. He also practised in Paris from 1916 to 1919. Dr. Gariepy was born in Montreal, completed his classical studies at L'Assomption College and his medical course at the University of Montreal, where he graduated in 1907. He practised medicine for a few years at Cap Chat in the Gaspe district. He is the last surviving member of his family.

Dr. William E. Glass, aged 40, of Hamilton, Ont., died suddenly on July 30 while on vacation at Port Rowan. He was president of Hamilton Academy of Medicine, and was well known and highly respected throughout the city as physician, citizen and former athlete.

Dr. Glass was born in Hamilton and lived all his life in this city, except when he was attending university doing postgraduate work, or serving in the Army. Following his graduation from Delta Collegiate he enrolled at Queen's University, where he graduated in medicine in 1935. On completion of postgraduate work in Montreal and London, England, he returned to Hamilton to open an office for general practice in 1939.

It was not long before he enlisted with the Fifth Field Ambulance, R.C.A.M.C., to go overseas in the Second World War, with the First Division, as a captain. He returned once to Canada to organize a mobile field ambulance unit at Camp Borden, and served with various medical units in the Italian campaign. In 1945 Dr. Glass returned to Hamilton following his discharge from the Army with the rank of major, to resume and rebuild his practice.

Dr. Guy Stewart Goodwin of Moose Jaw, a past president of the Canadian Medical Association, died in Vancouver, B.C. on July 8. Dr. Goodwin, born in Halifax in 1891. He practised in Moose Jaw from 1921 to 1949, when he retired to Vancouver. He served in the Royal Army Medical Corps from 1914 to 1919. Between the First and Second World Wars he was officer commanding the 10th Field Ambulance in Moose Jaw. He was founder of the Associated Medical Clinic in that city. Survivors include his widow, a son and a daughter.

Dr. Zadok Hawkins, aged 71, of South Ohio, N.S., died on July 23. Although in failing health, he was active in his profession until shortly before his death being ill only a very short time. Born in Pennfield, N.B., Dr. Hawkins received his early education in Sussex, N.B., and his medical degree from McGill University.

After graduation he went to Yarmouth County where he remained in continuous practice of medicine for 43 years. He is survived by his widow and one son.

Dr. Gordon P. Jackson, aged 66, Toronto's medical officer of health for the past 22 years, died of a heart attack at his summer cottage on August 14. Born in Elora, Dr. Jackson was educated in Toronto at Alexander Muir and Queen Victoria Public Schools, Parkdale Collegiate and University of Toronto. After graduation, he went to Montreal to serve for a year as superintendent of Western Hospital there; then followed five years of general practice at Wroxeter.

From 1917-19 he was a captain in the Canadian Army Medical Corps. On his return he joined the staff of the Department of Public Health. In the 1919 smallpox epidemic he was assistant diagnostician in smallpox. In the fall of 1921 he became diagnostician and medical examiner, and in 1924 was appointed chief diagnostician and director of quarantine and communicable diseases.

In 1929 when only 44 years old, he became head of the department. Under Dr. Jackson's vigorous direction, the successful toxoid anti-diphtheria campaign was carried on in the city. He also led in a longtime "war" on tuberculosis. His championing of the right to disseminate birth control information was not so successful, however.

In World War II he acted as director of medical services for the Civilian Defence Corps for Toronto. This year he was named deputy director of medical services for civilian defence in the metropolitan area. Dr. Jackson leaves his widow and one son.

Dr. Jean Perrin, who had the uncommon distinction to graduate as a lawyer and doctor, died after a long illness at his home in St. Lambert, Quebec on August 20. He was in his 39th year. He practised law for two years after graduating from Laval University in Quebec and then took up medicine at the University of Montreal where he graduated last year. He had been practising his new profession when he was seized with illness. Born at Pierreville, he attended St. Laurent and St. Marie colleges. He later attended McGill University and then Laval University for his law degree.

After serving his clerkship with the firm of Brais and Campbell, he was admitted to law practice and joined the firm of Duguay and Carignan. Dr. Perrin had a liking for medicine. He gave up his law practice and attended the University of Montreal. Dr. Perrin is survived by his widow and three daughters.

Dr. Leonard E. Rice, aged 86, who practised in Toronto from 1890 to 1918, died on August 13 at the Queen Elizabeth hospital. Dr. Rice graduated from Trinity Medical College, University of Toronto, in 1890, and later took postgraduate work in California. He spent his last several winters holidaying in Jamaica. Dr. Rice is survived by his widow.

Dr. Beverly W. Robertson, aged 77, of Fredericton, N.B., died on July 31, at Victoria Public Hospital of cerebral hæmorrhage. He was born in Queens County, and graduated from Provincial Normal School in 1893. For some years he taught school there and obtained his medical education from McGill University, graduating in 1905.

For a year he practiced medicine at Hatfield Point, then moving to Keswick Ridge, where he developed a large practice. In 1946 Dr. Robertson suffered a badly broken leg, spending some weeks in Victoria Public Hospital, and the following winter in Florida. Thereafter his activity gradually declined until the time of his final illness. He is survived by his widow and one son.

Dr. James Arthur Smith, aged 68, prominent Vancouver medical specialist died on July 2. Dr. Smith obtained his early education in New Westminster, then went to McGill University for his medical training. He played for the famous Salmonbellies lacrosse team in the great days of "Grumpy" Spring.

Dr. Smith was B.C.'s leading eye, ear, nose and throat specialist. After graduating at McGill, he took further training at the Manhattan eye, ear, nose and throat hospital in New York. At the time of his death he was president of the eye, ear, nose and throat section of the B.C. Medical association.

He is survived by his widow and two sons.

Dr. John J. Wall of Ottawa, died on August 10 at his summer cottage at Big Whitefish Lake, near Poltimore, Quebec, after a prolonged illness. He was in his 56th year.

Born in Ottawa, he was educated in this city. Following his graduating from McGill University in 1923, he interned for a year at the Royal Victoria Hospital, Montreal. Following this he spent a year at Dr. Shirley's Hospital in Detroit.

Starting in 1925, Dr. Wall spent three years in postgraduate studies at Vienna, specializing in eye diseases. Following his return from Europe, he was employed by the Department of Indian Affairs until his retirement in 1939. While with that department he travelled extensively in Northern and Western Canada.

on call

published in the interest of community medical service

An indication that a national health insurance scheme for Canada can become a reality soon has come from official Ottawa sources.

In an article in a current issue of *Maclean's,* a leading Canadian national magazine, Blair Fraser has said that the establishment of a pension scheme has now made planning for national health the next logical move. And as though to recognize already the difficulties which must attend the organization of a health scheme, the federal government has committed itself to form a parliamentary committee which will investigate the possibilities of such a plan. The committee is scheduled to start its work in 1952.

Mr. Fraser, regarded as one of Canada's top interpreters of the political scene, has many contacts in Ottawa which make his statements most reliable. Noted for his accuracy in reporting and knowledge of political movements at Ottawa, Mr. Fraser has been quoted at length on different occasions by many outstanding publications. He has taken the rôle of a radio commentator on national networks in Canada several times.

He states that the government move to form a committee was perhaps aided by the fact that the Canadian Medical Association decided at its annual meeting in Montreal to ask for formation of Trans-Canada Medical Services. Later, during a House debate on health insurance, Prime Minister Louis St. Laurent commented:

"Several members of the government as Canadian citizens, myself included, have noted with great interest the reports of these (C.M.A.) proposals and have welcomed this further evidence of the concern of the medical profession in Canada to increase the efficiency and scope of their assistance to their fellow citizens . . . I think that circumstance is all to the good . . . I have no doubt that all levels of government will be most anxious to see them succeed in this undertaking and to consider with them what part this government should take in helping to make the plan succeed and extend to the whole population." This was on June 20.

The CCF party thereupon made objection, and asked Mr. St. Laurent if the government had abandoned plans for a national health insurance scheme. The reply was given by Minister of Health and Welfare, Paul Martin. He said: "We (meaning the government) are giving consideration to the matter—to set up a parliamentary committee to examine this whole problem."

(This statement thus indicated a change of mind in Ottawa, since, on May 29, in House sessions, Mr. Martin, when queried by Mr. Stanley Knowles, member for Winnipeg Centre, on whether or not the government was considering the setting up of such a committee, replied: "I answered that question earlier this session. The answer is no.")

One fact which is apparently still very much in the minds of those in government in Ottawa is that health, as a Canadian problem, is essentially a provincial concern. For that reason, the setting up of a plan, Mr. Fraser feels, is not as imminent as it might appear. Before such a program could be put into effect, complete and lasting agreement would have to be obtained between the federal government and the ten provinces. And undoubtedly one of the most significant points in the development of health insurance is the part which doctors will play. Recognition of this was made by Mr. Fraser. "Certainly, the profession will have to be consulted at every step," he said.

He continued to say that a variance of opinions will not make the lot of the parliamentary committee any easier. There are those who feel that the first link in the chain of national health insurance is concerned with hospital care. Such a beginning, Mr. Fraser feels, will be popular in political circles, since it can hardly create any enmity on any side. The public will be happy with it, it is assumed that the doctors would not vigorously object to it, and, by government standards, it would be relatively easy to administer. Public support should be forthcoming, because the scheme for hospital insurance should relieve many of the financial burdens incurred in the various hospitals across Canada.

Yet it appears that there will be some opposition to that. A few comments have been made that hospital insurance should be the last to be considered, and that a general medical plan must be first. It is being argued, according to Mr. Fraser, that too many advantages would be taken of the hospital plan, and that the institutions would become over-crowded with patients clamoring for attention which might have been better given at home.

Much of the history of national health insurance dates back to the Dominion-Provincial conferences of 1945. Since that time, a great deal of work has been done in surveys of health requirements and problems in each of the ten provinces. All the surveys are expected to be on hand, completed, in Ottawa, by October.

Mr. Fraser's comment includes a statement that most provincial governments do not want such a plan. Only two, British Columbia and Saskatchewan, can be counted on for any support. Balancing that argument is the fact that a number of provincial prime ministers were not in favour of pensions, either. When they

heard the demands of the people, however, they listened and acted.

Above all, any decisions of the parliamentary committee will be brought to a Canadian Cabinet, which, in Mr. Fraser's words, is "sceptical" of the program.

Realization that the doctors must have a hand in the formation of the plan is encouraging. It means that men having a direct interest in making the finest medical care available for the most Canadians will have an opportunity of suggesting the sound basis they believe should be incorporated in the program. With more than a 38% increase for 1950 in participation in plans providing medical care and sponsored by medical or hospital groups in Canada as evidence, and with enrollment in plans jumping 41% in the same year, such schemes are rapidly assuming a permanent part in Canadian family expenditures and planning.

The agreement by the government to appoint a committee indicates to an even greater degree the work that must be done by the Canadian Medical Association and Canadian doctors. If national health insurance is definitely in the future, the job of doctors and their association will be to lend all the co-operation and help they can to the planners.

The health of Canadians is of prime importance. For that reason, a national health insurance plan, if it must be established, must cater to the particular needs of Canadians, and must pattern itself after their way of life. Therefore, the experiment in progress in Great Britain can have little bearing on any Canadian proposal. It may provide a few conclusions, but should not be taken as a mould from which Canadian national health insurance might be shaped. In addition, there is an evident awareness among those responsible for planning the nation's health insurance that the medical profession in Canada is deeply concerned with two objectives. First, that Canadian physical well-being be provided for by fine medical care; and second, that the plan will be a financial success for both patient and plan. These goals are proof that Canadian doctors realize that the health and welfare of Canadians today can foreshadow the progress and prosperity of the nation in years to come.

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en devoir

Publié par l'Association médicale canadienne dans l'intérêt des soins médicaux en commun

Une indication que le plan d'assurance de santé nationale pour le Canada peut devenir bientôt une réalité, a été divulguée de sources officielles à Ottawa.

Au cours d'un article récent paru dans MacLean's, l'un des magazines les plus importants au Canada, Blair Fraser énonça que le plan de pension établi actuellement, suscite un plan de santé nationale, comme suite logique du premier. Comme le gouvernement reconnaît déjà les difficultés que doit rencontrer l'organisation d'un plan de santé, le gouvernement fédéral a formé un comité parlementaire qui étudiera les possibilités d'un tel plan. Ce comité doit commencer son travail en 1952.

M. Fraser, reconnu comme l'un des analystes les plus éminents de la scène politique canadienne, possède plusieurs relations à Ottawa, ce qui donne beaucoup de valeur à ses écrits. Reconnu aussi pour son reportage exact et sa connaissance des événements politiques à Ottawa, M. Fraser a été cité au long à différentes occasions par plusieurs publications importantes. Il a plusieurs fois joué le rôle de commentateur à la radio, sur les réseaux nationaux du Canada.

Il explique que le geste du gouvernement de former un comité fut peut-être aidé par le fait que l'Association Médicale Canadienne décida, au cours de sa réunion annuelle à Montréal, de demander l'organisation de services médicaux Trans-Canada. Plus tard, à l'occasion d'un débat à la Chambre des Communes au sujet de l'assurance-santé, le Premier Ministre l'Honorable Louis St-Laurent s'exprime en ces termes:—

"Plusieurs membres du gouvernement, en tant que citoyens canadiens, moi-même y compris, ont manifesté beaucoup d'intérêt à l'égard des rapports sur ces propositions (A.M.C.), et ont accueilli avec enthousiasme cette preuve additionnelle de l'intérêt démontré par la profession médicale pour augmenter l'efficacité et l'étendue de ses soins à l'égard des citoyens . . . Je crois que ces circonstances sont très favorables et je ne doute pas que tous les services du gouvernement seront très anxieux de voir les médecins réussir dans leur plan et considéreront avec eux quel rôle le gouvernement peut jouer pour aider au succès de ce projet et l'étendre à toute la population."

Ces paroles furent prononcées le 20 juin.

Le parti CCF posa une objection et demanda à l'Honorable St-Laurent si le gouvernment avait abandonné le plan d'un système national d'assurance-santé. Cette question fut répondue par le Ministre de la Santé et du Bien-Etre l'Honorable Paul Martin qui dit:— "Nous (le gouvernement) donnons beaucoup de considération à un tel plan pour établir un comité parlementaire qui examinera le problème au complet.

(Ces paroles indiquent donc un changement d'opinion à Ottawa puisque le 29 mai, au cours de la session, M. Martin, questionné par M. Stanley Knowles, député de Winnipeg Centre qui demandait si le gouvernement avait l'intention ou non de former un tel comité, répondit: "J'ai ré-

pondu déjà à cette question au début de la session. La réponse est non.")

Un fait cependant demeure présent à l'esprit de nos législateurs à Ottawa, qui semblent croire que la santé est un problème de la législation provinciale. Pour cette raison, l'établissement d'un tel plan croit M. Fraser, n'est pas aussi éminent qu'il semble. Avant qu'un tel programme puisse être effectué, un accord complet et durable doit être obtenu entre le gouvernement fédéral et les dix gouvernements provinciaux. De plus l'un des points les plus significatifs dans le développement d'un plan d'assurance-santé est le rôle que les médecins peuvent jouer. M. Fraser reconnaît ce fait d'ailleurs en disant: "La profession devra certainement être consultée pour chaque développement."

Il ajoute que la différence des idées ne rendra pas la tâche plus facile au comité parlementaire. Certains pensent que le premier pas à faire dans le domaine de l'assurance-santé nationale concernant les soins dans les hôpitaux. Un tel début croit M. Fraser, sera très populaire dans les cercles politiques puisque ce domaine ne peut susciter beaucoup d'opposition d'un côté ou l'autre. Le public l'acceptera favorablement, les médecins ne montreront sans doute aucune objection et selon les organismes du gouvernement, ce plan serait relativement facile à administrer. Le public devra cependant contribuer son soutien car un tel plan devra relever les hôpitaux dans tout le Canada, des charges financières onéreuses qu'ils doivent supporter.

Pourtant, il existe une certaine opposition à ce programme. Quelques commentaires ont été émis et expriment l'avis que l'assurance-hôpital doit être considérée en dernier et qu'un plan médical général doit d'abord être établi. Il a été dit aussi dans certains milieux, selon M. Fraser, que trop de gens voudraient profiter des nombreux avantages offerts par un plan d'assurance-hôpital et que ces institutions deviendraient encombrées par des patients réclamant des soins qui en d'autres circonstances, pourraient être donnés à la maison.

Beaucoup des pourparlers au sujet du plan d'assurance-santé nationale, remontent aux conférences fédérales-provinciales de 1945. Depuis cette date, beaucoup de travail a été accompli par des enquêtes sur les besoins de la santé et sur les problèmes qui existent dans chacune des dix provinces. Tous ces rapports seront complétés et présentés à Ottawa au mois d'octobre.

Le compte-rendu de M. Fraser indique que la plupart des gouvernements provinciaux ne veulent pas d'un tel plan. Seules la Colombie-Britannique et la Saskatchewan donneront sûrement leur support. De plus plusieurs ministres provinciaux n'étaient pas en faveur du plan du pension, mais en constatant les demandes du peuple, ils ont écouté et agi.

Au-dessus de toutes ces considérations, les décisions du comité parlementaire seront portées à l'attention du Cabinet Canadien qui selon les mots de M. Fraser, est "sceptique" à l'égard de ce plan.

Il est encourageant de réaliser que les médecins auront une part active dans l'organisation de ce programme. Ce fait signifie que des hommes directement intéressés à donner aux Canadiens les meilleurs soins médicaux, auront l'occasion de suggérer la base solide qu'ils croit devoir incorporer dans un tel organisme. Avec une augmentation de plus de 38% en 1950 dans la participation de ces plans prodiguant des soins sous l'égide des médecins et des hôpitaux au Canada, et avec un enrôlement dans ces plans atteignant 41% au cours de la même année, ces mêmes plans jouent de plus en plus un rôle important dans l'économie familiale des Canadiens.

L'acceptation par le gouvernement de nommer un comité indique à un degré encore plus grand le travail qui doit être accompli par l'Association Médicale Canadienne et les médecins au Canada. Si le plan d'assurance-santé nationale se réalise dans l'avenir, le travail des médecins et de leur association sera de donner toute la coopération et l'aide qu'ils peuvent à ceux qui préparent ce plan.

La santé des Canadiens est de première importance. Pour cette raison, un plan d'assurance-santé nationale, s'il doit être établi, doit pourvoir aux besoins particuliers des Canadiens et établir un programme en accord avec leur façon de vivre. Voilà pourquoi le plan actuel qui se développe en Grande-Bretagne, peut avoir très peu d'influence sur tout plan canadien. Il peut offrir quelques points, mais ne peut être envisagé comme une copie d'après laquelle le plan d'assurance-santé au Canada devrait être préparé. De plus, ceux qui sont responsables de l'organisation de ce plan d'assurance-santé nationale, réalisent que la profession médicale au Canada, possède deux objectifs importants. Premièrement, que le bien-être physique des Canadiens soit pourvu de soins médicaux attentifs, et deuxièmement, que ce plan soit un succès financier et pour les patients et pour le plan.

Ces buts indiquent donc que les médecins canadiens réalisent que la santé et le bien-être de leurs concitoyens aujourd'hui, laissent prévoir le progrès et la prospérité de la nation pour les années à venir.

MEDICAL SUNDAY AT ST. GEORGE'S CHURCH, MONTREAL, SUNDAY, OCTOBER 21, AT 11 A.M.

The address will be delivered by the President of the Montreal Chirurgical Society, Dr. A. T. Henderson, and the scripture lessons will be read by Dr. A. D. Campbell and Dr. W. W. Francis. Representatives of the medical profession and associated professions are cordially invited.

NEWS ITEMS

Forthcoming Meetings

CANADA

Ontario Public Health Association, 2nd Annual Meeting, Royal York Hotel, Toronto, Ont., October 1-2, 1951.

Saskatchewan Hospital Association, Hotel Saskatchewan, Regina, Sask., October 11-12, 1951.

British Columbia Hospitals' Association, Hotel Vancouver, Vancouver, B.C., October 16 to 19, 1951.

Associated Hospitals of Manitoba, Winnipeg, Manitoba, October 24 to 26, 1951.

Ontario Hospital Association, Royal York Hotel, Toronto, Ont., October 29 to 31, 1951.

Canadian Public Health Association, Christmas Meeting of the Laboratory Section, Royal York Hotel, Toronto, Ont., December 17-18, 1951.

UNITED STATES

American Society of Clinical Pathologists, Annual Meeting, Chicago, Ill., October 15, 1951.

American Public Health Association, 77th Annual Meeting, Civic Auditorium, San Francisco, Calif., October 29 to November 2, 1951.

American Society of Plastic and Reconstructive Surgery, Annual Meeting, Colorado Springs, Co., October 31 to November 2, 1951.

The American College of Surgeons, 37th Clinical Congress, Civic Auditorium, San Francisco, Cal., November 5 to 9, 1951.

Pan-Pacific Surgical Association, Fifth Congress, Honolulu, Hawaii, November 7 to 19, 1951.

The Radiological Society of North America, 37th Annual Meeting, Palmer House, Chicago, Ill., December 2 to 7, 1951.

American Medical Association, Clinical Session, Los Angeles, Calif., December 4 to 7, 1951.

OTHER COUNTRIES

European Society of Hæmatology, Third Congress, under patrongae of the Hæmatological Society of Italy, (Dr. M. Torrioli, Via Genova 24), Rome, October 3 to 6, 1951.

World Federation for Mental Health, Mexico City, Mexico, December 6 to 12, 1951.

International Congress on Mental Health, Mexico City, Mexico, December 11 to 19, 1951.

Fourth Pan-American Congress of Ophthalmology, Mexico City, Mexico, January 6 to 12, 1952.

Alberta

The new wing of the University of Alberta Hospital was opened with an appropriate ceremony on September 4, 1951. This new wing adds three hundred and five beds to the now nine hundred and twenty-five bed hospital. The addition has all the modern conveniences of such an institution. Dr. A. C. McGugan is Superintendent of the University Hospital, and has played an active part in new additions to the hospital in recent years.

Dr. Morris Weinlos of Edmonton is attending the International Surgical Society in Paris and will be returning to his practice in October. Dr. Weinlos served with the R.C.A.M.C. overseas from the commencement of hostilities and retired from the service as Colonel.

Dr. Cameron Harrison, a Fellow of the Royal College of Surgeons is now associated with Dr. Roy Anderson in General Surgery in Edmonton. Dr. Harrison served with the R.C.A.M.C. during the war.

The graduates of the 1941 medical class held their reunion in the Mcdonald Hotel of Edmonton, on August 30 and 31. A 75% attendance was recorded. Each member of the class contributed the sum of twenty dollars to a fund to be administered by the Dean of Medicine of the University of Alberta to needy medical students during their last two years. We hope that other classes will follow the fine example now set by the class of 1941. Dr. Gordon Blott of Nanaimo, B.C. is president and Dr. C. G. McNeil of N. Vancouver is Secretary of the class.

W. C. WHITESIDE

British Columbia

The new British Columbia Academy of Medicine Building has been completed, and has been turned over to the College of Physicians and Surgeons by the architects. The Library of the Vancouver Medical Association is now in process of moving from its former home in the Medical-Dental Building downtown, and the offices of the College and the Canadian Medical Association (British Columbia Division) are occupied by their respective staffs.

The new Academy Building, which of course, is the property of the College of Physicians and Surgeons, and so of the whole medical profession of the Province, is a very fine building, and will be the home of the various medical organizations for many years to come. Its design is simple but most practical, with a maximum of efficiency and comfort. In addition to offices and Committee Rooms, there is a large Board Room, capable of subdivision, and the basement contains a large lounge or "rumpus room", luxuriously furnished, and providing accommodation for meetings and social events.

It is the hope of the College to have an adequate auditorium as part of the Academy, and land immediately adjoining the present building has been bought which will eventually be used for this purpose.

A good deal of other building for medical and hospital purposes is going on just now in B.C. Thus there is the new extension of the British Columbia Cancer Institute in Vancouver. This is a reinforced concrete and stone building, with space for the new radiological equipment of the Institute both diagnostic and therapeutic, and accommodation for bed patients. This will greatly help the work of the Institute, which has been very badly cramped for room.

Again, the new 264-bed sanitarium for the treatment of tuberculosis, now being built in Vancouver by the Provincial Government, will very greatly advance the plans of the Division of Diseases of the Chest, and will relieve the serious bed shortage in this department. It will be ready for occupation early in 1952, and will be the last word in up-to date efficiency.

Dr. Gordon F. Kincade, Director of Tuberculosis Control for B.C., states that this building will provide plenty of space for all who need bed treatment. Dr. Kincade succeeds, in this position, Dr. William H. Hatfield, who for so many years, has headed tuberculosis control in the Province, and has recently been appointed adviser to the Provincial Government in matters concerning chest diseases and tuberculosis. He has made very great contributions to the progress of this whole cause, and leaves a trail behind him of work accomplished which will be hard to follow. The crown, to some extent, of his achievements is represented by the magnificent B.C. tuberculosis Institute, one of the finest things of its kind on the continent. Dr. Hatfield surrounded himself with a most able corps of assistants, and British Columbia now has men whose work in medicine and surgery of the chest is the equal of any to be found. Dr. Kincade, his successor, has for many years, been his right hand man, and no better man could have been chosen to succeed Dr. Hatfield.

St. Vincent's Hospital in Vancouver, too, as we understand, is to increase its bed capacity in the near future by some hundred beds. This hospital, the latest comer to the hospitals of Vancouver, is operated by the Sisters of the Immaculate Conception, and has rapidly come to be recognized as one of the best hospitals in the city. It is a matter of general rejoicing by the medical men of Vancouver that it is to be enlarged.

Dr. William C. Gibson, director of research for the Crease Clinic in New Westminster, and associate professor of neurological research at the University of British Columbia, will attend the International Congress on Poliomyelitis in Copenhagen, shortly to be held. He represents the National Foundation for Polio, B.C. Division, and will be the only Canadian physician, officially at least, at the Conference. His trip will be financed by the B.C. Polio Fund, sponsored by that most generous and public-spirited organization, the Kinsmen's Clubs of B.C., who have been behind so many projects designed to advance medicine and medical knowledge and treatment. Thus they made a gift last year to the U.B.C. of an electron microscope costing some $10,000, and they have contributed largely to the B.C. Rehabilitation Institute for Paralytics and Spastics—and also to the B.C. Medical Research Institute.

Dr. Gibson, while in Europe, will also visit centres of research on diseases of the nervous system, notably the Karolinska Institute in Stockholm, Sweden.

The Parliamentary Committee of Enquiry, appointed to investigate and report on the workings of the B.C. Hospital Insurance Act, is now fully at work, and has spent the past few weeks travelling round the whole province, and holding meetings at which the fullest opportunity is being given to all connected with the administration and working of hospitals, to express their opinions and tell of their experiences with the Act. The newspaper accounts of these meetings have been very full, and in the writer's opinion at least, very fair and objective. Two things seem so far to emerge very clearly —the first being the fact that everyone seems to be wholeheartedly in favour of the idea of hospital insurance — and the second, that there is a great deal of dissatisfaction and heartburning over many of the details of its administration. It would seem only fair to say that the officials in charge of the administration have a very difficult job to do, and are doing the best they can as they see it—but there seems to be a very grave lack of elasticity and little attempt to grasp the needs and problems of hospitals and patients alike. So many of the complaints seem to be about mistakes and defects that could have been avoided by more sympathetic consideration. In any case, there is no doubt that this enquiry will be of great benefit, both to the Government and to the public. The Committee expects to close their tour with a week or so of hearings in Vancouver and the Lower Mainland, and Victoria and its environs..

J. H. MACDERMOT

Manitoba

The Children's Hospital, Winnipeg, opened a Speech Therapy Clinic on August 15, under the direction of Dr. Robert MacNeil.

Dr. Otylia Sobel, a graduate of the University of Pisa, Italy, who recently successfully completed a year's rotating internship in Saskatoon City Hospital, is now Senior Intern at Manitoba Sanatorium, Ninette.

Dr. S. L. Carey has received an award from the Fenton Bequest for his paper "How Serious is Our Readmission Problem," prepared for presentation at the Canadian Tuberculosis Association annual meeting in May at Toronto.

Our congratulations are extended to Dr. J. Wendell Macleod who will succeed Dr. Lindsay as Dean of the Faculty of Medicine of Saskatchewan University. Dr. Macleod was an outstanding student at McGill and has been highly successful in the practice of internal medicine. Manitoba's loss is Saskatchewan's gain.

Dr. John R. Judge, who graduated in 1950, and his wife have left for Pangnirtung, N.W.T. where Dr. Judge will be in charge of the Anglican Hospital for Eskimos.

Dr. A. W. Hicks has retired from practice at Roblin and has been succeeded by Dr. Edward Otke.

Dr. W. L. Bell, London University, has taken over as medical director of the Brandon Health Unit.

ROSS MITCHELL

New Brunswick

Dalhousie Medical School, Halifax has announced that members of the Medical Faculty of the University will give lectures in the four Maritime Provinces during the coming winter. A poll of physicians in each province will decide the subjects for these lectures most desired by the practicing doctors. Dalhousie will supply this extramural service as an addition to their annual refresher courses for Maritime doctors. The plan was decided upon following consultation between the University and the Medical Societies of Nova Scotia, Newfoundland, Prince Edward Island and New Brunswick.

Dr. James A. Lewis, son of the late Dr. A. A. Lewis of Saint John, joined the R.C.A.M.C. after graduation from Dalhousie University this year. He served during the Second World War with the 14th Field Ambulance.

Dr. Frank Stuart has been appointed to the permanent medical staff of the Lancaster Hospital, Department of Veterans' Affairs.

Dr. Glenn MacDonald has resumed practice in Saint John after a long postgraduate study in Pediatrics.

A. S. KIRKLAND

Nova Scotia

Dr. P. S. Campbell, Deputy Minister of Health and Welfare for Nova Scotia, has retired after an outstanding career of thirty-five years as physician and Provincial Health Officer. Born at Port Hood in 1881, Dr. Campbell graduated from St. Francis Xavier University in Arts and after a further year of Science there he took up engineering. Had it not been for the closing down by flooding of the Port Hood mine some years later, Canada might never have had her most prominent medical health officer. Out of work when the mine closed he went to McGill to further his engineering studies and there was won back by what had been his first love, medicine. In 1916 he graduated with the degree of M.D., C.M. Dr. Campbell was resident physician at Montreal General Hospital from 1916 to 1918. He engaged in private practice in Port Hood from 1918 to 1923, then entered the service of the Provincial Government. He soon came to be recognized as an authority in the rapidly growing field of public health and his keen perception, his broad understanding of his field, coupled with the unwavering soundness of his judgement made him an invaluable servant of his province and indeed of the whole country.

During the war years Dr. Campbell was decorated with the O.B.E. in recognition of his labours. On his retirement he received presentations from Premier Angus L. MacDonald and from Dr. William Forest of Ottawa representing the Dominion Council of Health.

Branch Societies of the Nova Scotia Division in annual meetings elected their slates of officers for 1951-52. At Yarmouth the Western Nova Scotia Medical Society elected: President, Dr. W. C. O'Brien; Vice-Presidents, Dr. R. E. Brannen, Clark's Harbour, Dr. P. H. LeBlanc, Little Brook; Secretary-Treasurer, Dr. D. F. MacDonald; Executive, Dr. G. V. Burton, Dr. P. E. Belliveau.

At New Glasgow the Pictou County Medical Society elected: President, Dr. C. B. Smith; Vice-President, Dr. J. B. MacDonald; Secretary-Treasurer, Dr. S. D. Dunn; Representatives to the Medical Society of Nova Scotia, Dr. A. E. Blackett and Dr. Hugh F. MacKay.

At Middleton the Valley Medical Society elected: President, Dr. J. R. McCleave, Digby; Vice-President, Hants County, Dr. G. W. Turner, Windsor; Kings County, Dr. H. A. Foley, Canning; Annapolis County, Dr. B. R. Wilson, Middleton; Digby County, Dr. D. G. Black,

Digby; Secretary-Treasurer, Dr. R. A. Moreash, Berwick; Representative to the Cancer Committee, Dr. E. S. Cochrane, Wolfville; Representative to the Executive of the Medical Society of Nova Scotia, Dr. F. R. Morse, Lawrencetown; Program Committee, Dr. J. E. Hiltz, Kentville, Dr. O. R. Stone, Bridgetown, Dr. R. A. Moreash.

The Bridgewater baseball team defeated Lunenburg 9—3 and in the process opened the fifty thousand dollar financial campaign for the new Lunenburg community hospital.

Dr. Donald I. Rice, (Dal. '51) has opened an office for general practice in association with Dr. John Slayter, Halifax.

Pictou Medical Society at its annual meeting introduced a resolution regarding the Registered Nurses Association Act of 1950, to wit:

WHEREAS The Medical Men of this Country give hundreds of hours annually to the Nurses Training School, and throughout the Province, Medical Men give thousands of hours annually to Training Schools. It is obvious that we have a vital interest in the standards of these Schools.

AND WHEREAS The cost of the operation of the Training School is a direct charge against the total revenue of the Hospital, which Hospital can only meet increased costs in the School by increasing its rates to the Public.

AND WHEREAS Legislation enacted in 1950 as "The Registered Nurses Association Act 1950" will, in our opinion increase such costs without providing additional revenues, and sets up standards which the Aberdeen and presumably other Hospitals cannot, at this time, comply with, as personnel are not available.

AND WHEREAS It would appear that the Registered Nurses Association of Nova Scotia is endeavouring to set itself up as a governing board for all Nurses Training Schools in the Province, without reference to the Boards of Trusts of the individual Hospitals, or the Medical and Teaching Staffs or same, or The Medical Society of Nova Scotia, or The Provincial Medical Board.

BE IT THEREFORE RESOLVED That this Medical Society views with concern actions taken by The Registered Nurses Association of Nova Scotia, which directly involve Nurses Training Schools in which Medical Men do practically all the advanced teaching.

AND FURTHER RESOLVED That this Resolution be passed to The Medical Society of Nova Scotia, and to the other branch Societies, with the request that the matter be considered at the next meeting of the Executive Committee of The Medical Society of Nova Scotia.

A medical team from Halifax commanded by Lieut.-Commander R. H. Roberts was dispatched to Malta to aid in the battle against an outbreak of poliomyelitis aboard the Canadian aircraft carrier *Magnificent*.

ARTHUR L. MURPHY

Ontario

The sixth annual meeting of the Association of Medical Illustrators will be held in Toronto October 1, 2 and 3 under the presidency of Mr. Natt C. Jacobs, Rochester, N.Y. The Association has a membership of one hundred from all parts of the United States and Canada. Miss Maria Wishart, head of the Department at the University of Toronto is charge of local arrangements. An exhibit of medical illustrations will be shown at the Hospital for Sick Children. Among the items on the program will be a demonstration of stereoscopic drawing by Mr. Lee Allan, Department of Ophthalmology, University of Iowa.

Dr. R. I. Harris, Toronto, is to deliver the Max Broedel Memorial Lecture. Other speakers are Dr. Harvey Agnew on "The Broader Relationships of Medical Illustration"; Pauline Burr Thomas, Wayne University, Detroit, Michigan on "Application of Modern Art Principles to Medical Art"; Ernest F. Hiser, University of Oklahoma on "Methods of Preparing Simple Animations".

The Right Honourable Sir Earle Page, K.C., M.G., F.R.C.S., Commonwealth Minister for Health, Australia, addressed the Toronto Academy of Medicine on "The Health Services in Australia".

The Ontario Department of Health announced that until the end of August there have been 722 cases of poliomyelitis in the province, giving a rate of 15 per 100,000 population. In 69% of the cases paralysis has not occurred. Fatalities have been 3.3% of cases.

The Faculty of Medicine, University of Toronto, has announced the following appointments and promotions: Professor of Pathology and Head of the Department, Dr. John Hamilton; Professor of Bacteriology and Head of the Department, Dr. P. H. Greey; Professor of Biochemistry and Head of the Department, Dr. A. M. Wynne, M.A.(Queen's), Ph.D.(Tor.); Professor of Biochemistry, Dr. Charles Hanes; Professor Emeritus of Biochemistry, Dr. H. Wastneys; Professor of Biochemistry, Dr. G. C. Butler; Professor of Physiology, Dr. E. A. Sellars; Professor of Hygiene and Preventive Medicine, Dr. F. O. Wishart.

In the Department of Medicine Dr. K. J. R. Wightman has been promoted to associate professor in Therapeutics, Dr. E. J. Maltby to associate professor and Drs. K. G. Gray and J. G. Dewan to associate professors in Psychiatry, Dr. J. W. Graham is assistant professor, while these have been made associates: Dr. A. F. W. Anglin, Dr. C. R. Burton, Dr. A. M. Doyle, Dr. C. C. Gray, Dr. W. F. Greenwood, Dr. I. M. Hilliard, Dr. A. H. Squires.

In the Department of Obstetrics and Gynæcology Dr. W. T. Noonan has been made associate professor. Assistant professors are: Dr. W. A. Dafoe, Dr. D. N. Henderson, Dr. H. W. Johnston. Dr. W. H. Murby is an associate. In the Department of Surgery assistant professors are: Dr. C. Aberhart, Dr. A. W. Farmer, Dr. F. P. Dewar. Dr. J. L. Russell is an associate. Dr. J. V. Basmajian is assistant professor in Anatomy as is Dr. W. Paul in Pharmacology. Dr. J. F. A. Johnston is associate in Ophthalmology and Dr. W. L. Donohue and Dr. C. R. McLean are associates in Pathology.

Dr. L. A. Pequegnat has been appointed successor to the late Dr. Gordon P. Jackson as Toronto's medical officer of health. After graduating from University of Toronto in 1919 Dr. Pequegnat interned a year at the Toronto General Hospital then did private practice for five years when he was class assistant in biology and assistant in anatomy at University of Toronto. Later he received a training grant from the Rockefeller Foundation which enabled him to obtain his diploma in public health from the School of Hygiene. In 1929 he was appointed deputy MOH and director of medical services. He is the author of several scientific papers.

H. Ward Smith, B.A., M.Sc., Ph.D., has been appointed director of the provincial crime detection laboratory, established to assist all police forces in Ontario. For the past six years Dr. Smith has been carrying on research in alcohol in biological fluids. He has done a survey concerning alcohol and its relation to traffic accidents which he presented at last year's international conference on the subject in Stockholm.

The laboratory will be located in the Old Sick Children's Hospital. Dr. Smith will work in collaboration with Professor Joslyn Rogers, consultant in pharmacology and with Dr. Noble Sharpe and Dr. W. L. Robinson who are attached as consultants in pathology.

LILLIAN A. CHASE

News from the University of Western Ontario

Under the will of the late John Bayne Maclean, $100,000 was bequeathed to the University to establish the Michael Francis Fallon Memorial Chair of Clinical

Preventive Medicine. Dr. George Edgar Hobbs, Assistant Dean of the Faculty of Medicine, has been named to occupy this chair.

Dr. James A. F. Stevenson, formerly of Yale University, has been appointed Professor and Head of the Department of Physiology, as of July 1, 1951. Professor Stevenson is known for his work on the hypothalamus. His research interests lie in the broad field of integrative physiology. He succeeds Dr. R. L. Noble, who continues as Professor of Medical Research and has been promoted Associate Head of that Department. Professor Noble has also been named Honorary Lecturer in Physiology.

A radioactive isotope laboratory has recently been established in the Department of Biochemistry by a grant from the Ontario Cancer Foundation, in conjunction with the University. This laboratory, which was approved in April by the Department of National Health and Welfare for ordering and handling isotopes, is now engaged in active work. It has a twofold program: fundamental research, in which any of the other Departments may participate; and diagnostic and therapeutic service for Victoria Hospital.

In the Department of Medical Research, of which Professor R. L. Noble has become Associate Head, Drs. C. R. Engel and K. K. Carroll have been named Assistant Professors, Dr. R. J. Rossiter, Professor and head of the Department of Biochemistry, has been designated Honorary Lecturer.

Dr. P. P. Hauch has been promoted from Instructor in Radiology to Lecturer, and Dr. M. B. Hill has been appointed Instructor in Radiology (St. Joseph's Hospital).

Dr. C. A. Thompson has been promoted from Instructor in Ophthalmology and Otolaryngology to Assistant Professor. Dr. R. E. Greenway has been appointed G. A. Routledge Fellow in Otolaryngology.

Dr. G. G. Copeland has been named Assistant in Obstetrics and Gynæcology and Dr. G. W. Prueter Fellow.

Dr. W. C. Sharpe has been promoted from Instructor in Medicine (tuberculosis) to Assistant Professor of Medicine.

The Dr. F. R. Eccles Memorial Medical Alumni Lectureship is scheduled for Wednesday and Thursday, October 3 and 4, 1951. The principal guest speaker will be Dr. Frederick A. Coller, Professor of Surgery, University of Michigan.

Quebec

Dr. Henri Ey, Psychiatrist-in-chief of the Bonneval Psychiatric Hospital of Bonneval, France, will give at the Prevost Sanatorium, Montreal, a series of 12 lectures on present-day psychiatric problems and 2 off-schedule lectures on general topics related to Psychiatry during October.

Dr. Ey is considered among the most authoritative exponents of to-day's psychiatric trends in France. His works represent his original as well as traditional interpretation of Psychiatry. The subjects he has chosen to discuss with dates of presentation follow: Psychiatry and the Evolution of Medical Sciences (Oct. 3); Doctrinal trends of today's Psychiatry (Oct. 5); Organodynamic conception of Psychiatry (Oct. 8); Evolution of ideas on Schizophrenia (Oct. 10); The thought and the personality of Schizophrenic (Oct. 12); Primary delusional experiences (Oct. 15); Chronic delusional organizations (Oct. 17); The neuroses (Oct. 19); Pathological Anxiety (Oct. 22); Hysteria and Psycho-somatic Medicine (Oct. 24); The theoretical and practical problems of Psychoanalysis (Oct. 26); Necessity and Limitations of Psychotherapy (Oct. 29).

The off-schedule lectures are: Psychiatry and Morals (Oct. 11); French Psychiatry of the XXth Century (Oct. 18).

Those wishing to attend the lectures should write to the Sanatorium Prevost, 4455 Gouin Boulevard West, Cartierville. An interpreter will be present.

Saskatchewan

The Saskatchewan Health Survey Committee has completed its work and the report is now being studied by the Government. The Committee was composed of 12 members. Dr. F. D. Mott, Deputy Minister of Public Health, and Dr. M. G. Taylor, Ph.D., Director of the Division of Research and Statistics, represented the government and acted as Chairman and Secretary respectively. Five members were chosen from representative sections of the public, and five others were chosen from the health professions, *viz.*, medical, dental, nursing and hospital.

Twenty-five one or two day meetings were held over the past two and one-half years. The report is being published in two volumes.

The University of Saskatchewan has announced the appointment, effective July 1, 1952, of Doctor J. Wendell Macleod to be the new Dean of the Faculty of Medical Sciences. The present Dean, Dr. W. S. Lindsay, will retire at that time after a long and honoured service.

G. GORDON FERGUSON

General

Immunization for travelers going to every section of the world are detailed in a booklet just released by the U. S. Public Health Service. The title of the booklet is "Immunization Information for International Travel". The booklet may be purchased from the Superintendent of Documents, Government Printing Office, Washington, D.C., for 20c a copy. A 25% discount is allowed on orders of 100 copies or more delivered to the same address.

The Board of Regents of the American College of Chest Physicians offers a cash prize award of two hundred and fifty dollars to be given annually for the best original contribution on any phase relating to chest disease. The prize is open to contestants of other countries as well as those residing in the United States. The winning contribution will be selected by a board of impartial judges and the award, together with a certificate of merit, will be made at the forthcoming annual meeting of the College. Second and third prize certificates will also be awarded.

In submitting a manuscript the following conditions must be observed: (1) Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, not later than April 1, 1952. (2) The only means of identification of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

Effective August 10, 1951, the office of the American Board of Obstetrics and Gynæcology will be located in Cleveland, Ohio. All communications should be addressed to Robert L. Faulkner, M.D., Secretary-Treasurer, 2105 Adelbert Road, Cleveland 6, Ohio.

Twenty-three hospitals in Ontario and Quebec are now using telecarts—telephones installed on wheeled carts—to provide service for patients confined to bed.

Telecarts were originally developed by the Bell Telephone Company for use in military hospitals for the convenience and comfort of hospitalized veterans. So gratifying were the results, in the opinion of hospital authorities, that their use soon spread to public wards of civilian hospitals as well.

At present 13 civilian and 10 military hospitals have telecarts available for their patients. The largest civilian installation is at the Royal Victoria Hospital in Montreal where there are 16; the military hospital with the most telecarts is Sunnybrook Military Hospital in Toronto which has 24.

Hospitals using telecarts have reported that the portable telephones have done much to relieve the sense of isolation and loneliness so often experienced by patients in hospitals. Though bedridden, a patient has only to let the nurse know he wishes to telephone and within a few minutes the telecart is wheeled up beside his bed.

News of the Medical Services

Canadian Armed Forces

Surgeon Lieutenant R. B. Ramsey, R.C.N.(R.)—appointed ashore for duties in the R.C.N. Hospital at Esquimalt ,after thirteen months' service as Medical Officer aboard the Tribal Class Destroyer H.M.C.S. *Athabaskan*. It was an eventful year for the *Athabaskan* as she spent ten months under the United Nation Command in the far eastern waters off Korea.

Surgeon Lieutenant Walter M. Little, R.C.N.—was appointed to H.M.C.S. *Magnificent*, Canada's largest warship,August 2, 1951. The *Magnificent* sailed early in August to participate in manœuvres with U.S. and R.N. Forces in the Mediterranean.

Surgeon Commander D.M. Bean, R.C.N.(R.)—appointed H.M.C.S. *La Hulloise* August 11, 1951. This Frigate joined the H.M.C.S. *Crescent* and H.M.C.S. *Swansea* for a one month cruise to the U.K. waters.

Surgeon Lieutenant Commander J. W. Rodgers, R.C.N. —appointed H.M.C.S. *Ontario* as Principal Medical Officer August 30, 1951.

Surgeon Lieutenant Commander J. C. Gray, D.S.C., R.C.N.—appointed H.M.C.S. *Naden* as P.M.O. R.C.N. Hospital and Officer-in-Charge of Medical Branch School and on staff of Command Medical Officer as Hygiene Officer, August 30, 1951.

Brigadier W. L. Coke, O.B.E., C.D., Director General of Medical Services, Canadian Army, recently returned from a tour of the United Kingdom and Western Europe, during which he visited the War Office and the medical and training establishments in Great Britain and in the British, U.S., and French zones on the Continent. He officially attended the XIIIth International Congress of Military Medicine and Pharmacy held in Paris, June 17 to 23 and the 14th Session of the International Bureau of Military Medical Documentation held in Vichy, June 24 and 25.

Lieut.-Colonel P. A. Costin, R.C.A.M.C., formerly Canadian Army Medical Liaison Officer, Washington, D.C., is attending the forthcoming course at the Canadian Army Staff College, Kingston, Ontario.

Lieut.-Colonel E. E. Tieman, O.B.E., R.C.A.M.C., formerly Area Medical Officer, Western Ontario Area, Central Command has been appointed Command Medical Officer, Eastern Command, with Headquarters at Halifax, N.S., exchange posts with Lieut.-Colonel R. B. Murray, R.C.A.M.C., who has now commenced duty at London, Ontario.

The new Wainwright Military Hospital with capacity of 100 beds, was opened June 21, 1951.

Major L. Lavallee, R.C.A.M.C., has been posted to the Brooke General Hospital, U.S. Army, at Fort Sam Houston, Texas, where he has been granted an assistant residency in surgery for a year. Major R. Feuiltault has obtained a similar year's residency in internal medicine at the same hospital. Major K.D. McQuaig, R.C.A.M.C., has been selected to attend the forthcoming course leading to the Diploma in Public Health at the School of Hygiene, University of Toronto.

The third R.C.A.F. para-rescue training course has commenced at Edmonton and is the first to include women. Two R.C.A.F. Medical Officers, Squadron Leader D. O. Coons and Flight Lieutenant J. R. Wynne and five nurses—Flying Officer A. Peden, Flying Officer L. M. Macdonald, Pilot Officer J. I. Thompson, Flying Officer M. D. E. Beaton and Pilot Officer M. F. Neiley are taking this course. In addition, nine other ranks are participating.

Thirty-five R.C.A.F. Medical Officers were present at the first indoctrination course for Regular Force Medical Officers held at the Institute of Aviation Medicine in Toronto from September 10 to October 3.

Wing Commander G. D. Caldbick, of the Directorate of Medical Services (Air), A.F.H.Q., is attending a course in Dermatology and Syphilology at the Harvard Postgraduate School of Medicine, Cambridge, Mass. His replacement at A.F.H.Q. will be Squadron Leader J. D. Munroe of Edmonton.

ABSTRACTS FROM CURRENT LITERATURE

Medicine

Stellate Block as an Adjunct to the Treatment of Pulmonary Embolism. Faxon, H. H., Flynn, J. H. and Anderson, R. M.: *New England J. Med.*, **244:** 586, 1951.

Stellate-ganglion block with procaine brought about an immediate relief of acute symptoms in three cases of pulmonary embolism where it was employed within a few hours of onset. Little improvement was noted in a fourth case in which the block was done some hours after embolism had occurred.

Stellate-ganglion block is considered to be a valuable means of modifying the reflex spasm which immediately follows pulmonary embolism and, because of this fact, it probably diminishes the area of lung which becomes infarcted. NORMAN S. SKINNER

Untoward Reactions to Tests for Epinephrine-Secreting Tumours (Pheochromocytoma). Bierman, H. R. and Partridge, J. W.: *New England J. Med.*, **244:** 582, 1951.

There is a growing tendency to employ pharmacologic tests for pheochromocytoma in the routine investigation of patients with hypertension. It is important to recognize that these tests are not without danger and should be carried out with due regard to the possibility of severe untoward reactions to the testing substance.

The authors encountered four severe, nonfatal reactions in 56 such tests on 21 patients. The use of 933F caused an elevation of blood pressure above 300 mm. of mercury in one patient and produced acute pulmonary œdema in another. Dibenamine caused anuria for fourteen hours in a third case and a marked hypotensive reaction followed a test with tetraethylammonium bromide in a fourth patient.

NORMAN S. SKINNER

The Rice Diet in Ambulatory Patients with Essential Hypertension. Loofbourow, D. G., Gallahan, D. and Palmer, R. S.: *New England J. Med.*, **244:** 577, 1951.

As the result of a careful clinical study of the effects of the rice diet on 105 patients in the Hypertension Clinic of the Massachusetts General Hospital the authors conclude that, in ambulatory patients, it produces no better results than does conservative medical therapy.

The rice diet is simple to follow and has psychological value in the treatment of patients who are extremely anxious concerning their hypertension. The diet is by no means innocuous and may even be lethal if the patient is not carefully followed. The monotony of the diet may cause recurrent depression and may give rise to overt hostility.

The rice diet would only seem to be indicated in certain patients who are severely ill with hypertension. In such cases it may bring about marked clinical improvement. NORMAN S. SKINNER

Perforated Peptic Ulcer: A Study of the Indications for Nonsurgical Treatment in Selected Cases. Vaughan, R. H. and Warren, R.: *New England J. Med.*, **244:** 898, 1951.

Patients with perforated peptic ulcer should usually be operated upon and it is logical to defer surgery only in the rare cases where the perforation has sealed, the peritonitis has become localized or when the patient is a poor surgical risk.

Of the 1,616 patients treated for peptic ulcer at the Veterans' Administration Hospital, West Roxbury, Massachusetts, over a six year period, there were 81 cases of perforation with three deaths. One death occurred in the 70 operated patients and two in the non-operative group of eleven patients. NORMAN S. SKINNER

Extract of Licorice for the Treatment of Addison's Disease. Groen, J., Pelser, H., Willebrands, A. F. and Kamminga, G. E.: *New England J. Med.*, **244:** 471, 1951.

Extract of licorice is commonly used as an adjuvant for disguising the taste of drugs in medical mixtures and also as a sweet for children. It has been reported as having value in the treatment of gastric ulcer, while its effect in the therapy of duodenal ulcer was considered doubtful. About 20% of the cases of peptic ulcer receiving extract of licorice developed hypertension and œdema or cardiac asthma or both, and this was shown to be due to sodium retention and potassium loss similar to that which follows the use of desoxycorticosterone acetate.

Two cases of Addison's disease are reported in which the symptoms were successfully controlled by the oral use of extract of licorice. It is suggested that this drug, or its active principle, may assume an important rôle in the treatment of this disease. NORMAN S. SKINNER

Mercuric Bichloride Poisoning. Troen, P., Kaufman, S. A. and Katz, K. H.: *New England J. Med.*, **244:** 459, 1951.

Mercuric bichloride ranked sixth in a list of over 25 of the commoner toxic ingestants used in suicidal attempts by patients admitted to the Boston City Hospital from 1934 to 1946. There were 65 patients admitted during this period with the diagnosis of mercuric chloride poisoning and of these 54 were selected by the authors as suitable for study.

Ingestion of corrosive sublimate produces gastro-intestinal lesions which vary in degree from a mild gastritis to a severe necrotizing ulceration. Renal involvement is common, manifested in mild cases as albuminuria only but which may progress to an anuric state and uræmia.

Individual prognosis is excellent if no urinary abnormalities are evident within 24 to 48 hours of ingestion. If renal damage occurs, prognosis is still excellent if the urinary output remains good for three days. The best therapy of mercuric bichloride poisoning consists in the immediate administration of BAL and prompt gastric lavage. Carefully planned parenteral therapy is essential if anuria develops, and some form of dialysis may be indicated in the individual patient.

NORMAN S. SKINNER

The Vasodilator Effects of Priscoline in Patients with Ischemic Extremities. Rottenstein, H., Horiwitz, O., Montgomery, H., Sayen, A. and Siems, L. L.: *Am. J. M. Sc.*, **221:** 661, 1951.

Twenty patients with age range of 17 to 78 years and presenting arterial disease including arteriosclerosis, thromboangiitis obliterans and vasospasm were studied in comparison with a normal group of 9 individuals as to their responses to intravenous Priscoline administration. All showed flushing of the face. One patient with bronchial asthma tolerated the drug well and another who was in mild congestive failure showed no unfavourable reaction. There was a cutaneous digital dilatation and increased blood flow in most of the individuals tested and this was particularly marked in the case of those with arterial disease. The blood pressures tended to rise slightly, but some showed a moderate drop.

The authors consider the effect of Priscoline to be local rather than central and localized to the cutaneous vessels in site of action with corresponding small cardiac output change. They did not observe any relationship between "basal vascular tone" and the effect produced by the drug. G. A. COPPING

The Treatment of Urgent Cases of Paroxysmal Auricular Fibrillation. Hellman, E., Altcheck, M. R. and Enselberg, C. D.: *Am. J. M. Sc.*, **221:** 655, 1951.

Accepting the general teaching as to the relative harmlessness of auricular fibrillation *per se* the authors point out that the rapid rate may increase any tendency towards failure and advise that its treatment be considered a matter of emergency in such cases.

The paper presents the findings in 25 patients in whom 30 paroxysms were treated. They used the following schedule in their management of these cases and consider it bridges satisfactorily the indecision frequently arising between the choice of digitalis and quinidine. The treatment is started with a rapidly acting digitalis preparation given intravenously, such as ouabain, K-strophanthidin, lanatoside C or digoxin. If slowing follows within the hour full digitalization may be embarked upon, if not, quinidine should be given. Where congestive failure is present both quinidine and digitalis should be used.

The doses used were: Ouabain 0.5 mgm.; digoxin 1.5 mgm., followed by 0.5 mgm. 4 hours later; quinidine 5-dose courses of 0.2 to 0.4 gm. every 2 to 4 hours increased by increments of 0.2 gm. in subsequent courses. Quinidine was given orally. G. A. COPPING

Surgery

Diverticula of the Duodenum. Mahorner, H.: *Surgery*, **133:** 697, 1951.

True diverticula of the duodenum, that include all the layers of the intestine in their walls and do not encroach on the lumen, are very common, being found in 2% of fluoroscopic examinations. They are usually symptomless, probably in 98% of the cases. They may cause symptoms, due to distension or pressure or inflammation, of pain, nausea, vomiting, weight loss, diarrhœa, jaundice, pancreatitis or peritonitis from perforation.

The pain due to duodenal diverticulum is similar to that of gall-bladder attacks, but may resemble peptic ulcer. Extension into the head of the pancreas may cause obstructive jaundice, or pancreatitis and diarrhœa. Hæmorrhage from a diverticulum has been described. There are three cases of carcinoma in a duodenal diverticula in the literature.

Surgical interference should not be undertaken lightly. These lesions are seldom life-destroying. Many of these symptom-producing diverticula are covered by pancreas and even those that appear to be on the right side of the duodenum have their origin on the left. The duodenum may be opened and a finger inserted into the diverticulum, or it may be outlined by distending the duodenum with air. Many diverticula are perivaterian and it may be necessary to intubate the common duct. Sometimes the diverticulum is removed and sometimes inverted.

It is emphasized that duodenal diverticula should not be removed unless definite symptoms can be attributed to them. BURNS PLEWES

Peripheral Arterial Embolism. Veal, J. R. and Dugan, T. J.: **133:** 603, 1951.

Immediately the diagnosis of peripheral arterial embolism is made, measures to protect the involved limb should be undertaken. A sympathetic nerve block is done and preparations made for operation if there is no relief of pain and coldness within 30 minutes. If the results of sympathetic block are doubtful, embolectomy should be done, for though the limb may survive there will be definite handicapping. Anticoagulant therapy with heparin and dicoumarol is begun four hours after the operation and continued for a long time. In the 28 cases reported all were treated within 8 hours and often four hours after the embolic episode; 16 required embolectomy and 12 responded to conservative measures. Of the 16 operated upon, 13 were immediately successful, but over a longer period 2 out of the 16 died and 3 had an amputation.

The procedure of embolectomy is described. The difficulties encountered are not minimized: fracture of an arteriosclerotic artery, immediate recurrence of thrombosis, and tight dressings. Conservative treatment is also discussed. The rôle of anticoagulants in both methods of treatment is emphasized.

BURNS PLEWES

Dermatology

Treatment of Psoriasis with Undecylinic Acid by Mouth. Rattner, H. and Rodin, H.: *J. A. M. A.*, **146:** 1113, 1951.

Since February, 1949, when the first of Perlman's reports was published, the use of undecylinic acid has become a matter of acute interest not only to dermatologists but also to the family practitioner. Thanks to the daily and periodical press the public has heard about it as well. "Saturated, and unsaturated, higher fatty acids" have been adopted into pseudo-scientific jargon and remedies, stated to contain such substances, are being exploited by commercial firms and offered as cures not only for psoriasis but for all other skin ailments as well.

In view of the intractable nature of psoriasis, which also undergoes spontaneous remissions or intermissions, it seemed important to the authors to approach the question of the value of undecylinic acid in psoriasis without prejudice and investigate the results as reflected in the experience of a wide and representative dermatological field of observation. Side effects were recorded by nearly every observer—nausea, flatulence, vomiting, fishy aftertaste, diarrhœa and "heartburn" were commonest. A few reactions of allergic character were observed, and there were also some reactions of a serious character. The latter included hæmorrhage from a quiescent gastric ulcer, exacerbations of quiescent gout, auricular fibrillation, coronary pain, etc., all of which subsided on withdrawal and reappeared when the drug was again exhibited. In a significant number of cases the psoriasis was aggravated, in some instances progressing to the serious state of exfoliative dermatitis. The overwhelming opinion of more than half the dermatologists consulted who reported enough cases to give value to their findings was strongly critical, and their views expressed with unusual emphasis.

The authors' conclusions, based upon experience derived from the use of undecylinic acid by mouth in over 1,100 cases of psoriasis treated by about 75 dermatologists are unfavourable. However, in view of the fact that at the time of reporting the drug had been in use for less than 2 years, they offer this only as a "status report".

D. E. H. CLEVELAND

Treatment of Acne Vulgaris. Andrews, G. C., Domonkos, A. N. and Post, C. F.: *J. A. M. A.*, **146:** 1107, 1951.

This paper is devoted in general to a consideration of the value of estrogenic substances and antibiotics, and specifically to results achieved in treating 384 cases of acne for two years with these agents and without the use of x-ray irradiation. The authors consider that, while they have not divorced themselves from roentgen rays in the treatment of acne where they consider it specially indicated, the results observed show the superiority of their method over others previously in vogue.

They stress three concepts as being of fundamental importance and rely upon them as a result of their studies. (1) Simple cases, characterized by a seborrhœal flux, comedones and papules, can be cured by a low-fat diet, vitamin A and diethylstilbœstrol, care of the scalp and the usual sulphur-and-lime lotions. (2) In pustular, nodular and cystic cases there is a sensitization to staphylococcus; focal infection is an important and perhaps the principal factor. These cases, in addition to hormone therapy, are to be treated chiefly with sulfonamides or antibiotics and removal of focal infection. (3) The staphylococci responsible for the last-mentioned group of cases vary greatly in their susceptibility to the various antibiotics and sulfonamides. Penicillin was found to have little clinical effect, the best results being obtained with sulfadiazine, aureomycin and terramycin. Female sex hormones were given to patients of either sex and under careful clinical control untoward effects in boys as well as in girls were avoided.

The details concerning the manner in which the remedial agents were used and systemic measures and local treatment given are fully described. Not all will agree with some arguments presented, such as the rôle of focal infection, but the paper is a valuable summary of the authors' experience in handling acne which have in recent years been widely used by dermatologists, and which are not as novel or radical as the publicity which they have received in the daily press would suggest.

D. E. H. CLEVELAND

Book Reviews

Heart Disease: Its Diagnosis and Treatment. E. Goldberger, Associate Attending Physician, Montefiore Hospital, New York. 651 pp., illust. $12.00. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1951.

So many books have been written on the subject of heart disease that it is difficult to visualize the place for still another. Such theoretical considerations disappear, however, on reading Dr. Goldberger's refreshing approach to the subject. He has written a concise account of his field as a specialist clinician writing for non-specialist clinicians. His approach is sufficiently physiological to provide the reader with a working background while still concentrating on the clinical findings and therapy. He begins by discussing the examination of the cardiovascular system, stressing above all those meaningful findings which are readily elicited by the intelligent examiner armed only with five senses and a stethoscope. To these he then adds the major ancillary methods of examination—radiology and electrocardiography. In the case of the latter, he does not dwell over-long on theory but endeavours to present the essential practical points which every physician requires. Brief outlines of numerous specialized and somewhat experimental methods, such as cardiac catheterization, electrokymography and angiography are also presented in order to allow the practitioner to follow the lines of development in modern cardiological investigation.

With this firm foundation carefully laid, the order of the book then follows naturally through a discussion of cardiac symptomatology into the co-ordination of symptoms and elicited findings which form the well known cardiac syndromes. The last half of the book is then devoted to a systematic description of diseases of the heart and circulation with the stress always on the clinical approach to the patient and the method of handling him. In this section, the author's approach is particularly rewarding, since it is written from a personal bias, without dogma, and as one experienced person talking to a less experienced colleague. Dr. Goldberger does not attempt to preach, he simply details what he has found helpful and hopes that the reader may also find it useful.

Medical Treatment, Principles and their Application. G. Evans, Consulting Physician, St. Bartholomew's Hospital. 1464 pp., illust. $26.25. Butterworth & Co. (Canada) Ltd., Toronto, 1951.

Several English and two North American authorities have contributed to this text which covers the significant diseases that may be treated by medical means. It is so written that the practitioner will feel that the author of each section has met the particular disease himself and can be relief upon to have seen patients respond to the treatment he describes. A background for diagnosis and logical therapy is provided at the beginning of all sections by a discussion of the current concepts of the etiology of each disease. A very short bibliography at the end of the various sections provides a ready means for obtaining more detailed information. Sections which one might not expect to find are those dealing with Nuclear Physics, X-ray and Radium Therapy, Geriatrics and Rehabilitation.

Canadian readers may occasionally be somewhat dismayed at being given only the English name for certain proprietary preparations, chiefly in the vitamin and hormone fields. This dismay will probably be balanced by finding numerous exotic prescriptions that are so characteristically English. Many of the prescriptions are similar to those which frequently appear in *The Practitioner;* ones which the physician has always intended to copy and file. Here he may find the prescription he has been seeking to treat the worrisome patient with the stubborn symptoms. Such has been the experience of the reviewer on more than one occasion since the book came to hand.

Current Therapy—1951. Edited by H. F. Conn. 699 pp. $11.50. W. B. Saunders Co., Philadelphia; McAinsh & Co. Ltd., Toronto, 1951.

This is the second volume of the series and it resembles the initial one which appeared in 1950. On the whole it is very successful in its aim to provide an up-to-date reference for the practising physician. Only therapeutic material is included, except for occasional notes on diagnosis where this is considered an important part of treatment. The book is arranged in sixteen sections, each dealing with a separate system or group of diseases. A long and impressive list of contributors have written the individual articles, and many of the diseases are discussed by two authors so that the reader is offered a choice of methods. At times there is a lack of balance common to this type of book in which so many writers have participated. For example, the treatment of urolithiasis is accorded ten full pages, whereas the whole section on locomotor diseases, chiefly arthritis, is covered in five pages. The book is clearly printed on good paper, and is well bound. There is a useful roster of drugs and a good index.

Anatomy of the Nervous System. O. Larsell, Professor of Anatomy, University of Oregon, Medical School, Portland, Oregon. 520 pp., illust., 2nd ed. Appleton, Century, Crofts, New York, 1951.

There is little doubt that Professor Larsell's book is among the finest texts in this difficult and encyclopædic field. This is even truer of the 2nd edition where the introductory sections dealing with gross organization, embryology and neurohistology have been enlarged and made sufficiently detailed so that the student has a complete presentation. The style of the book is clear and straightforward, the illustrations profuse and very helpful. The technique of superimposing tracts and nuclei on figures of gross topography is particularly excellent. This enables one to have a three dimensional concept of the nervous connections.

The author follows a very lucid and logical order. He lays a careful basis of gross topography which is followed by a meticulous description of the elements involved, the effectors and receptors. These are the foundation stones upon which he then builds up a functional and structural description of the central nervous system. The last chapter concerns the vascular supply of the nervous system. This rounds out the logical sequence, for the importance of the vessels only becomes clear when they are projected against a knowledge of the function of the individual vascular territories.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Metabolic Methods, Clinical Procedures in the Study of Metabolic Functions. C. F. Consolazio, Chief of Biochemistry, United States Army, Medical Nutrition Laboratory, Chicago; R. E. Kohnson, Professor and Head of the Department of Physiology, University of Illinois; E. Marek, Biochemist, United States Army. 471 pp., illust. $7.75. The C. V. Mosby Co., St. Louis, Mo.; McAinsh & Co. Ltd., Toronto, 1951.

Lane Medical Lectures, Companionship of Water and Electrolytes in the Organization of Body Fluids. J. L. Gamble. 90 pp. $2.50. Stanford University Press, Stanford, California, 1951.

Wonderfully Made, Some Modern Discoveries About the Structure and Functions of the Human Body. A. R. Short, Professor of Surgery in the University of Bristol. 159 pp., illust. 6/- net. The Paternoster Press, Ludgate House, Fleet Street, London, 1951.

Spleen Puncture. S. Moeschlin, Privatdozent, University Medical Clinic, Zurich. 229 pp., illust. 30 s. net. William Heinemann, Medical Books Ltd., London, 1951.

In a Harley Street Mirror. R. S. Stevenson. 278 pp., illust. $3.75. Christopher Johnson, London; Ryerson Press, Toronto, 1951.

Electron Microscopic Histology of the Heart, An Application of Electron-Microscopic Research to Physiology. B. Kisch, Research Associate in Cardiology, Mt. Sinai Hospital, Professor at Yeshiva University, New York City; in collaboration with J. M. Bardet, Research Laboratories of the Inter-Chemical Corp., New York City. 106 pp., illust. $5.50. Brooklyn Medical Press, New York, N.Y., 1951.

CCH Canadian Income Tax Act, 17th ed. Consolidated to adjournment of Parliament, June 30, 1951. Including, the Canada-United States, Canada-United Kingdom and Canada-New Zealand Income Tax Agreements. 300 pp. $3.00. CCH Canadian Ltd., Toronto, Ont.

Ocular Toxoplasmosis. M. J. Hogan, Associate Clinical Professor of Ophthalmology and Clinical Director of the Francis I. Proctor Founation for Research in Ophthalmology, University of California Medical School. 86 pp., illust. $3.25. American Ophthalmological Society, New York; Columbia University Press, New York, 1951.

Transactions of the American Ophthalmological Society. Eighty-Sixth Annual Meeting, Hot Springs, Virginia, 1950. 702 pp., illust. $16.25. American Ophthalmological Society, New York; Columbia University Press, New York, 1951.

Good Health with Diabetes. I. Murray, Physician in Charge of Department for Metabolic Diseases, Victoria Infirmary, Glasgow; and M. B. Muir, formerly Sister-Dietician, Victoria Infirmary, Glasgow. 44 pp., 2nd ed. $0.45. Livingstone Ltd., Edinburgh; Macmillan Co. of Canada Ltd., Toronto, 1951.

Low-sodium Diet. T. B. Rice, Professor of Public Health, Indiana University School of Medicine, Indianapolis, Indiana. 103 pp. $3.30. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1951.

Visceral Radiology. E. Markovits, Scientific Collaborator of the Central Radiologic Institute of the General Hospital (Holzknecht-Institute) Vienna; Head of the Radiologic Department of Elizabeth Hospital of the City of Budapest. 612 pp., illust. $24.00. Macmillan Co. of Canada Ltd., Toronto, 1951.

Anæsthesia in General Practice. S. C. Cullen, Head of Division of Anæsthesiology, Department of Surgery, State University of Iowa Hospitals; Professor of Surgery (Anæsthesiology), State University of Iowa College of Medicine. 292 pp., illust., 3rd ed. $4.50. The Year Book Publishers Inc., Chicago, 1951.

Human Physiology. B. A. Houssay, Professor of Physiology; Director of the Institute of Biology and Experimental Medicine, Buenos Aires, Argentina; J. T. Lewis, Professor of Physiology; Director of the Institute for Medical Research, Rosario, Argentina, and O. Orias, Professor of Physiology; Director of the Mercedes and Martin Ferreyra Institute of Medical Research, Cordoba, Argentina, etc. 1118 pp., illust. $18.90. McGraw-Hill Co. of Canada Ltd., Toronto, 1951.

Large Scale Rorscharch Techniques. M. R. Harrower, Research and Consulting Phychologist, New York City; and M. E. Steiner, Research Psychologist, General Electric Co., Bdigeport, Connecticut. 353 pp., illust., 2nd ed. $10.25. Charles C. Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1951.

Lutte Antipaludique par les Insecticides a Action Remanente. E. J. Pampana, Chief de la Section du Paludisme, Organisation Mondiale de la Santé. 72 pp., illust. $1.00. Organisation Mondiale de la Santé, Palais des Nations, Genève, 1951.

Clinical Hæmatology. M. M. Wintrobe, professor of Medicine and Director, Laboratory for the Study of Hereditary and Metabolic Disorders, University of Utah, College of Medicine, Salt Lake City, Utah. 1048 pp., illust., 3rd ed. $15.00. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1951.

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